# THE OXYGEN SUPPLY TO THE HUMAN FOETUS

## and the Clinical Syndromes associated with Anoxia.

A THESIS

submitted for the Degree of Doctor of Medicine

by

JAMES WALKER, B.Sc., M.B. Ch.B. (Glas.) M.R.C.O.G.

Midwifery Department,
University of Aberdeen.

December, 1953.



ProQuest LLC.
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106 – 1346

# INDEX.

DISCUSSION.

APPENDIX.

# PREFACE.

The criterion of efficient reproduction is that after a pregnancy characterised by good health, the mother delivers unaided a healthy, fully formed and vigorous child.

Reproduction is a natural function but experience has shown that in very many instances pregnant women suffer some abnormality of pregnancy or labour, calling for special medical care, or fail to deliver a live or healthy child.

Failures in the physiology of a given pregnancy may be genetic or hereditary in origin or have their primary source in some feature of the environment of the mother or foetus. The presence of hereditary or genetic factors

is difficult to establish, but some are known to be responsible for foetal deformity (Needham, 1942). Their role and further importance remain to be assessed.

It is easier to study general environmental influences in mother or foetus, and such an investigation has been undertaken for the last five years in the Midwifery Department of the University of Aberdeen. It was hoped that study, by epidemiological methods, of normal and morbid pregnancy in a community might define the circumstances under which abnormalities occur and the population groups most likely to develop morbid states. Maternal environmental factors such as housing, diet, and social background affect the foetus indirectly through the mother, but their influence is difficult to assess. The mother's age, height and general health are immediate environmental factors for the foetus, and may be more easily measured.

A team consisting of a nutritionist, dietitians, social scientist, a psychologist and a statistician have, over the last five years, in co-operation with clinical obstetricians, studied the influence of such general environmental factors on the pregnant woman and on the clinical course of her pregnancy. The researches of this team (of which the writer is a senior member) cover a very wide field and approach problems from many angles. Whenever epidemiological studies define a clinical or

population group as more liable to some morbid state, a clinical or physiological investigation is planned to elucidate, if possible, the reason for such a connection. It was in this way that epidemiological studies of the environment of the foetus suggested the work of this thesis.

One of the main problems studied by the team was the "cause and nature of obstetric death" (stillbirths plus first week neonatal deaths). A series of such deaths occurring over a period of 14 years was studied and the causes of death were classified in a new way, taking into account the clinical circumstances of the case and the autopsy findings (Baird and Walker, 1954; Baird, Walker and Thomson, 1954). Amongst other factors, the effects of maternal age and parity, and of length of gestation, were studied in obstetric deaths as a whole and in various types of death. It was found that death of mature babies with, at autopsy, the non-specific lesions of anoxia alone, became much more common with rising maternal age in all parities and with prolongation of pregnancy after term. The association of anoxia with prolonged pregnancy taken together with the observations of Barcroft and Young (1945), that the oxygen supply to the postmature foetal rabbit fell progressively to very low levels, suggested that a similar defect in oxygen

supply to the human foetus might occur after term.

The work of this thesis shows that, in the human foetus, the supply of oxygen deteriorates gradually in the last few weeks of pregnancy and rapidly after term. In response to a falling oxygen supply the foetus produces an increased supply of red cells so that, at birth, the haemoglobin may be much above normal adult levels and the red cell count over 5.0 million per c.mm., much higher than the levels in the well oxygenated foetus.

Normal labour and, in many instances, prolonged or difficult labour has been found to have little effect on the oxygen supply. The supply is depressed where there is maternal pre-eclampsia and in some other abnormal conditions of pregnancy. Where the foetus passes meconium (foetal distress) the oxygen supply has been found to be very low indeed.

Statistical studies of "foetal distress" have demonstrated that the incidence rises sharply with advancing maternal age and with prolongation of pregnancy, and that this rise is due mainly to an increase in the number of foetuses who pass meconium.

Much of the epidemiological material presented with relation to obstetric death is necessarily the findings of the research team, but the writer has been a senior member of this

team from the start. He is solely responsible, however, for the method of presentation of the results and for the interpretations discussed in the thesis. Planning and execution of the investigation of oxygen levels and the study of "foetal distress" were the sole responsibility of the writer, and all laboratory estimations were performed personally except where otherwise stated.

ACKNOWLEDGMENTS.

The author owes a substantial debt of gratitude to the following people.

(1) To Professor Dugald Baird, who stimulated this research by his investigation into the causes of stillbirth and who has throughout the period of the work encouraged and guided the author by his interest and constructive criticism.

(2) To Dr. Angus M. Thomson (Special Research Lecturer, University of Aberdeen), who has given much help on the technique of epidemiological studies.

(3) To Dr. Elizabeth Turnbull (Garden Research Fellow, Midwifery Department, University of Aberdeen,) who has kindly presented some of her findings to complete the picture, and who has been of much technical assistance in the author's own studies.

(4) To clinical colleagues and the nursing staff of the Aberdeen Maternity Hospital who, by their co-operation, made a study of oxygen levels possible.

(5) To Mrs. Paton (Senior Records Officer) and her staff for material for statistical studies.

(6) To Mr. Gordon Adams (Senior Departmental Technician) for the photographs which illustrate the thesis.

(7) To many who, by their interest and advice at various stages of the work, have contributed to the end result, but in particular to:-

Dr. Isabella Leitch, Director, Commonwealth Bureau of Animal Nutrition;

Professor Clement A. Smith (Paediatrics), University of Harvard.

Professor J.H.P. Jonxis (Paediatrics), University of Groningen.

Professor R Brinkman (Biochemistry), University of Groningen.

# INTRODUCTION.

## FACTORS WHICH INFLUENCE THE OXYGEN SUPPLY TO THE FOETUS.

(A Review of the Literature)

In this introduction are reviewed previous studies of factors which influence the oxygen supply to the foetus. Few studies have been made on the human foetus but much information has been obtained from studies of other mammals.

The oxygen supply reaching the foetal tissues depends on many independent factors and previous work has therefore been reviewed under the following main heads.

(1) The Oxygen Content and Percent Saturation as found in the Blood of the Umbilical Vessels of the foetus.

(2) Factors influencing the supply of oxygen available at the maternal side of the placenta.

(3) The placenta as an organ of transfer.

(4) Factors influencing the uptake of oxygen by the foetus and the supply available to individual tissues.

(5) Foetal response to anoxia.

(6) Clinical manifestation of anoxia.

## (I) THE OXYGEN CONTENT AND PERCENT. SATURATION FOUND IN THE BLOOD OF THE UMBILICAL VESSELS OF THE FOETUS.

### (1) Observations on Animals.

In 1884, Cohnstein and Zuntz published the results of what was probably the first study of the oxygen content of the blood of the umbilical vessels of a mammalian foetus. They found, in five sheep foetuses, that the mean oxygen content of the blood in the umbilical vein and artery were 4.4 and 2 vols. per cent. respectively.

In 1927, Huggett, working with the goat foetus, found in six cases mean values of 7.96 and 2.94 vols. per cent. in blood of the umbilical vein and artery with ranges of 5 to 12 and 0.25 to 6 volumes per cent. respectively. The mean percentage saturation of the blood in the vein was 45 per cent. and in the artery 16.6 per cent.

In 1934, Barcroft et al, also working with the goat foetus, investigated the oxygen saturation of the blood of the foetuses at various times in the latter half of pregnancy. They showed that the saturation of the blood of the umbilical vein rose from 60 per cent. at the 10th week to 80 per cent. at the 16th to 19th week, and fell abruptly to 45 per cent. just before term (21 to 22 weeks). (Fig. 1). They quoted only the highest figures found by them at each period of gestation as they

considered their technique unreliable because the results varied so greatly, especially in the last two weeks. They made the very valuable observation that the percentage saturation with oxygen varied greatly with different periods of gestation. The percentage saturation, however, is not an independent variable as it depends upon the relation between the oxygen capacity and content of the blood.

Between 1935 and 1939, Barcroft studied the variations in oxygen content, capacity and percentage saturation of the blood of the sheep foetus during the latter half of pregnancy. This comprehensive study made a most important contribution to the knowledge of the physiology of oxygen supply to the foetus in utero. The results found (Barcroft et al, 1939b) are seen in Figs. 2 and 3. The authors conclude that:-

(a) The oxygen content in the umbilical vein rises slowly till the 85th day, is level till about the 120th day, and then gradually falls.

(b) The content in the umbilical artery is low up till the 90th day but from then till the 100th day there is a rise. From the 100th day the content falls, the fall becoming steeper as time goes on.

(c) The percentage saturation of the blood in the

umbilical vein rises to a maximum of about 90 per cent. from the 80th to the 100th day. From then on, the saturation falls to reach 65 per cent. at term (142 ± 2 days).

(d) The saturation in the artery gradually rises up till the 90th day, is high from the 90th to the 130th day and then falls steeply to be about 20 to 30 per cent. at term.

Roos and Romijin (1938) studied the oxygen content in the umbilical vessels of the foetal ox. The five foetuses investigated were born by elective Caesarean Section at from 7 to 8½ months of gestation. The oxygen content of the blood in the umbilical vein ranged from 6.3 to 9.8 vols.per cent. and that in the artery from 2.41 to 5.07 vols. per cent. The percentage saturation in vein and artery varied from 54 to 90 per cent. and 19 to 46 per cent. respectively.

Steel and Windle (1938) studied the foetal cat born by Caesarean Section in a saline bath. The oxygen content of the blood in the umbilical vein before the onset of respiration in 22 cases varied from 0.7 to 4.6 vols. per cent. Towards the end of gestation the maximum saturation of the blood of the umbilical vein was about 50 per cent.

Snyder (1949) studied the oxygen content in the umbilical vessels of 103 foetal rabbits, and his results are shown in Fig. 4. In the umbilical vein the oxygen content remains constant

at 12 to 13 vols. per cent. from the 25th to the 29th day, falls gradually in the next few days till term at the 32nd to 33rd day, and more rapidly in the postmature period when readings as low as 8 vols. per cent. may be found. The percent-:age saturation with oxygen in those three periods was 90 per cent., 78 per cent. and 54 per cent. respectively.

Barcroft and Young (1945) studied the effect of postmaturity in the rabbit somewhat more indirectly by estimating the oxygen content of the blood in the cerebral venous sinuses of foetuses at various stages of pregnancy from the 26th to the 36th day; where the pregnancies had been artificially prolonged. The percentage oxygen saturation is seen in Fig. 5. By the 36th day (3 to 4 days after term) it was insufficient to support life.

Conclusions that may be drawn from observations on animals.

(a) Unless the stage of gestation is quoted the determinations mean very little.

(b) The oxygen of the blood during pregnancy undergoes a series of well ordered changes which can only be understood by a consideration of the relations between oxygen capacity, oxygen content and percent. saturation at each stage.

(c) Results of readings at or near term are inherently variable and estimations of oxygen content show a wide scatter.

Summary of Findings.

(1) In the sheep, goat and rabbit foetus it has been demonstrated that the percentage saturation of the blood in the umbilical vein rises until a little after mid pregnancy. From then, the saturation remains at a high level till relatively near term, when it begins to fall, to reach levels at term which are about two-thirds those seen at earlier periods. In the rabbit, it has been demonstrated that the fall in percentage saturation continues if pregnancy is prolonged after term and the percentage saturation with oxygen of the blood reaching the foetal brain may be so low that the foetus may die in utero.

(2) The oxygen content of the umbilical vein blood in the sheep and rabbit foetus has been show to follow a similar pattern to the percentage saturation, but the fall preceding term is less than the fall in percentage saturation. The fall in content in the rabbit continues where pregnancy is prolonged beyond term.

(3) The oxygen content and per cent. saturation in the umbilical artery has been studied only in the sheep. Both content and percentage saturation are low up till mid pregnancy, and relatively high when the percentage saturation in the vein is high, and again low near term.

(2) Observations on the Human Foetus.

No carefully planned or comprehensive studies have been made of the oxygen levels in the blood in the umbilical vessels of the human foetus. The information available is derived from a series of isolated measurements concerned mostly with the situation at the time of delivery. In a few cases readings have been taken at elective Caesarean Section but nothing is known of the variations occurring during the course of pregnancy.

Blair-Bell et al (1928), while investigating the metabolic function of the placenta, studied the oxygen content in the umbilical vessels in seven foetuses at birth before the onset of respiration. The mean values found were 9.0 vols. and 5.8 vols. per cent. in the vein and artery respectively, but individual readings are not given.

Goldbloom and Gottleib (1930) studied the oxygen content and saturation in the umbilical vessels of nine foetuses after spontaneous delivery where inhalation anaesthesia had not been used. They found a mean oxygen content in the vein of 17.2 vols. per cent. and a mean saturation of 79.6 per cent.

Haselhorst and Stromberger (1930) in a series of five cases delivered by Caesarean Section under spinal anaesthesia before the onset of labour, found that the oxygen content of the

umbilical vein blood averaged 3.97 vols. per cent. (range 2.46 to 5.72) while that in the artery was 0.84 vols. per cent. In a further four cases delivered by the same means and reported in 1931, the same authors found the oxygen content of the umbilical vein blood to be 13, 12, 11 and 7 vols. per cent. respectively, (average 10.8 vols. per cent.) much higher read-:ings than their first and better known series. They also estimated the oxygen contents in the umbilical vessel of 22 infants at birth after normal spontaneous delivery conducted without anaesthesia. (Haselhorst and Stromberger, 1930). They found the average content in the vein to be 10.1 vols. per cent. (range 4.9 to 14.9 vols. per cent.) and in the artery 3.4 vols. per cent. (range 0.4 to 8 vols. per cent.) The saturation of the blood in the vein averaged 45 per cent.

In one case, an elective Caesarean Section at term performed under local anaesthesia, Eastman,(1930) found the oxygen content in the vein to be 13.3 vols. and the saturation 64 per cent. In the artery the content was 6.3 vols. per cent. In a study of ten infants born spontaneously without anaesthesia he found that the oxygen content of the umbilical vein blood averaged 10.5 vols.per cent. with a saturation of 50 per cent. The arterial blood contained 3.3 vols. per cent. of oxygen.

Haselhorst and Stromberger (1930), who found a mean content

of 3.97 vols. per cent. in the blood of the vein before the onset of labour and a mean content of 10.1 vols. per cent. after labour, concluded that normal labour enhanced the oxygen supply to the foetus. Eastman (1930) who found readings before and after labour to be 13.3 and 10.5 vols. per cent. respectively, concluded that normal labour depressed the oxygen supply to some extent. It will be noted that if Haselhorst and Stromberger had used their later series of readings (1931) to calculate the level before the onset of labour, they would have reached much the same conclusion as Eastman.

Noguchi (1936), in a study of "normal infants at birth," showed that the mean oxygen content was 10.2 vols. and 3.4 vols. in the vein and artery respectively.

Dieckman and Kramer (1944) studied the oxygen content of the umbilical vein in three foetuses delivered by elective Caesarean Section under local or caudal anaesthesia before the onset of labour. In the vein the contents were 6.13, 6.8, and 12.79 vols. per cent. and in the artery of two of the cases 2.14 and 2.6 vols. per cent.

Summary and Conclusions from Human Experiment.

(1) Where the human foetus is delivered near term by elective Caesarean Section, oxygen contents varying from 2.46 to 13.3 vols. per cent. have been found in the umbilical vein (Table I). Recent authors (Smith, 1945) accept the upper readings as more likely to be normal, and all investigators have found individual readings at or near 13 vols. per cent. The information available is scanty and it is not possible to draw any accurate conclusions of the state at term except to note the variability in readings similar to the variability seen in animal experiments.

(2) There is more agreement amongst different authors where the oxygen content of the umbilical vein blood is studied after spontaneous delivery without anaesthesia (Table II). The mean levels of the oxygen content of the blood in the vein are very close to 10 vols. per cent. in all series with a per cent. saturation of 50 per cent. The range, however, in any given series is wide.

(3) No information is available of the oxygen contents at various stages of pregnancy and no investigation has been made of the effect of abnormal pregnancy.

## (II) FACTORS INFLUENCING THE SUPPLY OF OXYGEN AVAILABLE AT THE MATERNAL SIDE OF THE PLACENTA.

### (1) Percent. saturation with oxygen of the maternal blood.

A deficiency of oxygen in the maternal blood may lessen the supply available to the foetus. The shift to the right of the maternal dissociation curve in late pregnancy (Fig. 10) tends to lessen the bad effect of a fall in maternal oxygen saturation but only to a very slight extent.

Much will depend on the type of anoxia. In the anaemic patient, even though the content of oxygen is low, the saturation and therefore the tension remains high. Bad effects, if any, arise from a deficiency in absolute amount of oxygen available. In the stagnant anoxia of the cardiac patient, the arterial oxygen is often high and bad effects, if any,on the foetus are due more to defects of circulation. It is in the anoxic anoxia group that the danger is real, as the oxygen saturation of the blood is low. In the normal pregnant woman, only with excessive sedation or anaesthesia is deficient arterial oxygen saturation likely to be seen (Lund, 1940). In the abnormal case, however, such a type of anoxia may arise. The patient with severe asthma and bronchitis, with cardiac shunts, or during an eclamptic fit, will have periods, long or short, during which the arterial blood has a lower saturation with oxygen.

Cyanosis appears clinically when the blood is from 75 to 85 per cent. saturated (the actual level depending on the acuity of the observer) (Comroe and Bothelo, 1947). A study of the dissociation curve (Fig. 10) shows that when cyanosis is clinically evident, the oxygen tension in the blood of the pregnant woman at term is only from 50 to 60 per cent. of the normal. In other words, with maternal cyanosis, the effective oxygen tension to the foetus is halved and it is probable that, under these circumstances, little transfer to the foetus can occur.

(2) The Oxygen Capacity of the Maternal Blood.

The oxygen capacity of the maternal blood in the pregnant mammal has been studied by many authors. Apart from the value of the observations in a study of maternal physiology of pregnancy, it was considered that the oxygen-carrying capacity of the maternal blood might have some influence on the oxygen supply to the foetus.

Roos and Romijin (1938) in a study of pregnant oxen, noted that in late pregnancy the oxygen capacity was below that of the non-pregnant animal. During delivery and after labour the oxygen capacity rose to at least non-pregnant levels.

Barcroft (1946) studied the oxygen capacity of the blood in a series of ewes before insemination and at the time of delivery of the lambs. His results, seen in Fig. 6, show that in early pregnancy, the blood of the ewe on an adequate diet

has a higher oxygen capacity than that of the non-pregnant animal. In late pregnancy the capacity falls and is at or below pre-pregnancy levels. As a result of an extensive study of the relationship between the oxygen capacity of the blood of the foetus and that of its mother (Fig. 7), Barcroft states:- "I have failed to discover any relationship between the mother and the foetus in terms of oxygen capacity of the blood."

(3) The Dissociation Curve of the Maternal Blood.

The ability of the maternal blood to transfer oxygen to her own tissues and to the foetus at various tensions depends on the dissociation curve.

Barcroft et al (1935) in a study of the dissociation curves of the blood of mother and foetal goats throughout pregnancy noted that from the 70th day onwards (i.e. just after mid pregnancy), the maternal curve was shifted to the right of that of the non-pregnant animal but the degree of inflection was about the same (Fig. 20). Barcroft (1946) quotes readings in two sheep. The first was 111 days pregnant and the second 152 days (normal gestation period in the sheep is 140 ± 2 days). The maternal curve of the second animal was well to the right of that of the first, but both were to the right of the normal. (Fig. 8). He attributes the shift to the right to an increase in the hydrogen ion concentration in the maternal blood in

pregnancy.

Roos and Romijin (1938) in a study of the maternal dissociation curve in one ox in the 8th month of pregnancy found the maternal curve within the normal limits for the non-pregnant animal. (Fig. 9).

Darling et al (1941) found that the dissociation curve of the blood of the pregnant woman at term lay to the right of that of the non-pregnant. This finding confirms earlier work by Eastman et al (1933) (Fig. 10) and Liebson et al (1936).

Conclusions:

It has been demonstrated that in the sheep, goat and human the dissociation curve of the maternal blood shifts to the right during pregnancy. A similar shift could not be demonstrated in the ox. The movement of the maternal curve facilitates the release of oxygen at all pressures. The curve is sigmoid in shape and the ability to release oxygen is therefore accentuated at low pressures.

(4) Maternal Circulation and Vascular Adjustments to Pregnancy.

As the uterus grows during pregnancy with the formation of a maternal placental circulation, a greatly increased vascular bed is produced. In the rabbit at the 28th day of gestation, the maternal vessels of the uterus contain about one-sixth of the total blood volume, (Barcroft and Rothschild, 1932). Similar information is not available for other species. In view

of the increased vascular bed, an increase in maternal blood volume is essential tomaintain an adequate circulation to the developing foetus. This will involve in addition an increase in cardiac output.

(a) Blood Volume. Caton et al (1951), using radio-active red cell techniques and performing serial invest-:igations in a group of pregnant women, have found:-

(i) There is an increase in total blood volume of 45 per cent. which is at its maximum some 60 days before delivery and then falls very slightly.

(ii) There is an increase in the total red cell mass of some 40 per cent. which is steady and continuous with its maximum at delivery.

(iii) There is an increase in the plasma volume of 55 per cent. which is at its maximum at 60 days before delivery and then falls slightly.

(iv) There are fairly marked individual variations both in degree of increase and time of maximum volume.

This work has extended that of Miller et al (1915), Dieckman and Wegner (1934), Thomson et al (1938), Roscoe and Donaldson (1946), and McLennan and Thouin (1948), all of whom had demonstrated somewhat similar patterns with dye techniques.

(b) Cardiac Output. The cardiac output increases steadily as pregnancy advances and the increase in output has been demonstrated by Hamilton (1949) using the Fick principle with auxiliary cardiac catheterisation. She shows a rise from the 10th week to reach a 25 per cent. increase by the 26th to 29th weeks. The output remains level for about 10 weeks to drop sharply after the 37th week to reach pre-pregnancy levels at term. (Fig. 11). The cardiac output is much raised in pre-eclampsia but not in hypertension alone. It is the increase in cardiac output which maintains the uterine circulation (Abramson et al, 1943), as there is in pregnancy no loss in circulation to other parts of the body.

(c) Maternal Arterial Blood Pressure and Effective Placental Pressure: Because of the altered haemodynamics in the presence of a placental vascular bed, there is a fall in maternal blood pressure in late pregnancy (Burwell, 1938).

Woodbury et al (1938) estimated the effective placental pressure by subtracting the intra uterine pressure from the maternal blood pressure (arm artery), both of which they measured. They found that in the first stage of labour the effective placental pressure was always positive, but in the second stage the effective pressure might be very low at the height of a bearing down effort. The increased intra uterine pressure of the second stage was compensated by a great increase in brachial artery pressure coincident with "bearing down" effort, otherwise

the effective placental pressure would have been negative. They state that occasionally at the height of bearing down, blood is forced backwards from the uterine arteries into the aorta, so that no blood reaches the placenta. (See Fig. 14).

(d) Uterine Vascular Adjustments. Barcroft and Rothschild (1932) found that the volume of blood in the uterus of the pregnant rabbit rises steadily till, at the 28th day about one-sixth of the total blood volume is in the uterine vessels. The actual amount depended on the amount of placental tissue. From the 28th to 30th days the volume of blood in the uterus is reduced by half, chiefly due to increasing distension of the uterine wall. According to Barcroft et al (1933), there is not a compensating increase in the rate of blood flow at this time. From the 27th day to term at the 32nd day, there must therefore be a decreasingly efficient circulation. Reynolds (1949) considered that the increased pumping action of uterine contractions at this time and a lessening distance between maternal and foetal bloods helps to compensate for the failing circulation.

Reynolds (1949) attributes changes in uterine blood flow both in rate and volume throughout pregnancy to alteration in shape and growth pattern of the uterus.

The findings and beliefs of Reynolds (1949, 1950),

Gillespie et al (1949), Gillespie (1950) and Ramsay (1949) from studies in the rabbit, monkey and human may be summarised as follows:-

(1) Growth of myometrium and of blood vessels is greatest in the first half of gestation, during which time the uterus is spherical in shape.

(2) In the second half of pregnancy, increase in size of the uterus occurs mainly by stretching. Blood vessels which were tortuous and grossly in excess of requirements pay out and become straight (Fig. 12).

(3) Near term, however, the blood supply is interfered with as the uterine wall becomes thinned by stretching, vessels reach the limit of elongation and tension in the uterus rises. It is to this latter picture that Reynolds attributes fall in uterine blood volume, rate of flow and efficiency of circulation at or near term. To this also is attributed the slowing or cessation of foetal growth about this time.

(e) Oxygen in Uterine Vessels. In 1935, Barcroft et al measured the amount of oxygen emerging in the blood of the uterine vein of the rabbit at various stages of pregnancy. They compared the results in the pregnant and the non-pregnant horn in the same animal. From the non-pregnant horn the saturation was 60 per cent. throughout. In blood from the pregnant horn the saturation rose to 80 per cent. in the first few days due

to hyperaemia, but fell steadily to 20 per cent. or less near term, returning to 80 per cent. after delivery (Fig. 13).

They considered that the extraction of most of the oxygen from the maternal blood as it passed through the uterus was evidence that the demand of the foetus for oxygen exceeded the ability of the mother to supply it. Where the pregnancy continued beyond term, the foetus obtained insufficient oxygen to enable it to survive (Barcroft and Young, 1945). Barcroft and his colleagues suggested that ultimate foetal death in the postmature was due to the demand of the foetus for oxygen outstripping the supply.

(5) The Effect of Maternal Anaesthesia.

Anaesthesia resulting in visible cyanosis will greatly reduce the oxygen available to the foetus because of oxygen deficiency alone, apart from any specific effect of the anaesthetic agent. There is also little doubt that oxygen deficiency short of visible cyanosis can occur (Comroe and Bothelo, 1947). Very little information is available about the effect of anaesthetic agents themselves on the oxygen saturation, circulation time, etc., of maternal blood in pregnancy.

(a) Effect on the Recipient Patient. In 1937, Shaw et al studied the effect of ether anaesthesia on the oxygen

levels in the arterial blood of dogs. They used a special modification (Shaw and Downing, 1935) of the technique of Van Slyke and Neill (1924) to prevent inaccuracies due to the presence of ether in the blood samples.

They found that (a) the oxygen capacity rose, (b) the oxygen content showed a slight rise, (c) the oxygen saturation showed a steady fall, (d) the content and saturation of the venous blood rose, and (e) the arterio-venous difference both in content and saturation fell.

McClure et al (1948) considered that some degree of anoxia may be an inevitable complication of anaesthesia, especially if interference with tissue respiration or histotoxic anoxia is part of the pharmacology of narcosis. They showed that during induction with pentothal in the human adequate oxygenation is only possible if at least 25 per cent. oxygen is given as well. With spinal analgesia, oxygenation is normal so long as the respiratory muscles are unaffected.

McQuiston et al (1943), investigating nitrous oxide analgesia in the human, found that with 20 per cent. oxygen, no serious anoxaemia resulted, the arterial blood being 85 to 95 per cent. saturated. Below that level of oxygen, (e.g. at 15 per cent. oxygen) serious anoxia occurred confirming the work of Sollman (1936), who showed that anoxia occurred with nitrous/

oxygen mixture whenever the oxygen was under 14 per cent.

(b) Effect on the Foetus of General Anaesthetics. In 1939, Smith studied the effect of ether, nitrous oxide and cyclopropane administered to the mother. He sampled maternal arterial and venous blood and blood from the umbilical cord of the foetus. The estimation of oxygen in blood samples containing anaesthetic gases is accurate only if special techniques are used. He utilised the modified techniques of Shaw and Downing (1935), and Orcutt and Waters (1937). He found (Table III) that ether did not depress the oxygen supply to the foetus unless given for a prolonged period, but that with both nitrous oxide and cyclopropane the levels of oxygen in the foetal blood were much reduced. He attributed the effect of cyclopropane on the foetus to the poor arterio-venous difference in the maternal blood. The maternal venous blood, being highly saturated with oxygen, has given up very little to the foetus.

Rovensteine et al (1940), using cyclopropane 25 per cent. at Caesarean Section, found the oxygen saturation of the blood in the umbilical vein of the foetus to range from 8 to 35 per cent. The maternal blood was fully saturated at the time.

Taylor et al (1951) investigated foetal blood oxygen levels at birth and in the first hour of life in 94 infants, where various anaesthetic agents had been used for short periods before delivery (See Tables III and IV). Their findings at the moment

of birth are comparable with those of Smith. Unfortunately they sampled the heel blood of the foetus and estimated the oxygen by the technique of Roughton and Scholander (1943), which, according to the authors, is invalid in the presence of anaesthetic gases.

In 1951, Watts et al studied the oxygen content of the umbilical vessels after maternal anaesthesia, (Tables III and IV). Blood was taken from an isolated segment of the umbilical cord immediately on delivery. They analysed the samples by the method of Van Slyke and Neill (1924), but did not state whether they took any of the technical precautions against the presence of anaesthetic gases which are essential to the accuracy of the result. These results, seen in Table III, are much higher than found by other investigators except for the readings of Goldbloom and Gottleib (1930) previously discussed (see page 7). Despite this, the relationships of their findings to each other are identical with those of other investigations.

(c) Effect on the Foetus of Spinal, Caudal or Local Analgesia.

The oxygen levels in the foetal vessels where the foetus is delivered spontaneously or by low forceps under spinal, caudal or local anaesthesia are seen in Table IV. It will be noted that the results are generally the same as where no anaesthesia is given, (Table III). The figures of Watts et al (1951) are again higher than others. Watts et al, however, noted that in eight of their

cases a drop in maternal blood pressure below 90 systolic occurred and in this group the percentage saturation of blood in the foetal umbilical vein was 20 per cent. lower than in cases where no such drop was noted. This effect is probably due to a fall in effective maternal placental pressure (see page 16).

The Effect of Added Oxygen. Where oxygen in high concentration is added to the anaesthetic agent or given during the course of delivery without anaesthesia or with local, spinal or caudal anaesthesia, the oxygen levels in the foetal blood are raised by 10 to 30 per cent. (Dieckman and Kramer, 1944; Batten, 1943).

The increase in the oxygen supply to the foetus by the exhibition of oxygen to the mother was first suggested on clinical grounds by Landais (1892) in her thesis and is an established clinical practice. The effect may be obtained in two ways. Firstly, before the exhibition of oxygen the saturation of the maternal blood might be below normal. No controlled experiments on the oxygen saturation of maternal blood during labour with or without anaesthesia, before and after administration of oxygen have been performed. It is, however, possible to increase above normal the oxygen saturation of adult arterial blood by the exhibition of 100 per cent. oxygen. It has been shown by Boothby (1938) that this result is achieved, firstly by full saturation of the haemoglobin and then by a greatly

increased carriage in solution in the plasma. The full effect is only obtained after 3 to 4 days, but then the blood is some 110-112 per cent. saturated. It is difficult to explain the rapid improvement in the foetus seen under clinical or exper-:imental conditions on this basis alone, but even a minor improvement in maternal oxygenation would be passed almost wholly to the foetus.

Summary.

The experimental results suggest that all anaesthetics studied may have a detrimental effect on the oxygen supply to the foetus. The only exceptions are ether, if used for only a very short time, and spinal or local, provided they are not accompanied by a drop in maternal blood pressure.

This "effect of anaesthesia" is a specific effect of the agent itself and assumes that the anaesthetic is properly administered.

Where the technique necessitates a lowering of the oxygen in the inspired mixtures, or is faulty and cyanosis appears, the effect on the foetus may be very great indeed and in the presence of deep cyanosis it is likely that no oxygen whatsoever is passed to the foetus.

(6) The Effect of Labour.

The findings following spontaneous delivery without anaesthesia have been noted already (page 8 ), and compared with the findings before the onset of labour. Eastman (1930)

suggests that a fall of saturation of about 10 per cent. occurs during spontaneous normal delivery but that the foetus is still well oxygenated. Haselhorst and Stromberger (1930) reach the opposite conclusion, but did not discuss the implications of their 1931 findings.

Where the foetus is born asphyxiated, the oxygen levels have been found to be very low. Eastman and McLane (1930) in six cases, found a mean content of oxygen in the blood of the umbilical vein of 1.3 vols. per cent., and Wilson, Torry and Johnson (1937) in nine cases a mean of 2.0 vols. per cent.

The effect of prolonged and difficult labour on oxygen content has not been studied in itself but only where asphyxia has supervened.

Williams (1952) suggests that relaxation of the uterus between contractions is essential to foetal oxygen supply as the intra uterine pressure may rise to 90 mm. of mercury in the first stage and to 180 mm. in the second, at the height of contractions. If the intra uterine pressure is above 80 mm. of mercury for more than 1 minute in every 5 minutes, the foetus will show clinical evidence of anoxia (Fig. 14).

Caldeyro-Barcia and Alvarez (1952) consider that the main danger to the foetus occurs when there is a high resting pressure in the uterus between contractions, interfering with adequate blood supply to the placenta. They have shown that foetal anoxia occurs if the resting pressure is above about 35 mm. of mercury as seen in some forms of abnormal uterine action.

## (III) THE PLACENTA AS AN ORGAN OF TRANSFER.

All nutrients reaching the foetus must be transferred across the placenta to reach the foetal circulation. The foetal portion of the placenta may itself be inefficient and act as a barrier to transfer.

### (1) Growth and Anatomy.

The growth of the human placenta and its structural characteristics have long been studied. The embryological development (Hertig and Rock, 1941, 1945, 1949; Hamilton, Boyd and Mossman, 1945) has been thoroughly examined and explained. Advances in knowledge of the later stages of human placentation have not kept pace with contributions to the knowledge of early development.

Calkins (1937) has shown that the weight and area of the placenta increases as pregnancy progresses, but that the rate of growth is relatively much less in the last third of pregnancy and that this slowing up is progressive. Hamilton and Boyd (1951) also find increased growth of the placenta which is rapid up to the 7th month. Christoffersen (1934) estimates the area of contact between villi and maternal blood at 10 to 13 sq. metres. Hamilton and Boyd (1951) have recently investigated the detailed histological structure of the placenta in situ and have suggested that the anatomical arrangement of the villi is labyrinthine. This confirms the opinions of Stieve (1940, 1942, 1948) and refutes the concept of Spanner (1935). The relationship of the

maternal arteries and veins to the intervillous space has not been finally decided. Spanner (1935) considered that the arteries opened through the basal plates but that the venous blood drained up to the chorionic plate and then laterally to be collected in a marginal sinus. Hamilton and Boyd (1951) could find no evidence of a marginal sinus but found that the veins drained through the basal plate into an extensive decidual venous plexus and that the arteries likewise pass from a decidual plexus through the basal plate, near the septa, into the intervillous space. This confirms to some extent the concept of Bumm (1893).

(2) The Placental Membrane.

Hamilton and Boyd (1951) state - "In the human placenta this term is used to designate the full thickness of the foetal tissue which separates the maternal blood in the intervillous spaces from the foetal blood in the capillaries of the villi. It is a membrane of unusual complexity. During the course of gestation the membrane varies greatly in its thickness ..... ....From the fifth month until term the placental membrane consists of the endothelial lining of the foetal capillary, an attenuated layer of mesenchyme, and the syncitio-trophoblast. The membrane varies in thickness in different regions of a given placenta, but it may be as thin at the fifth month as at the ninth month."

The histology of the membrane has been studied (mainly in late pregnancy) by Wislocki and Dempsey (1946), Wislocki et al (1948) and they have found that after the 33rd week the syncytium begins to degenerate and in some areas will appear only as a homogenous plate. Superficially a fibrin deposit appears on the membrane. At term, according to Tenney and Parker (1940), some 10 to 50 per cent. of terminal villi show degenerative changes. Excessive calcification is said to occur in the ageing placenta, but Masters and Clayton (1940) could find no increased evidence of calcification in postmature placentae though calcification was not normally seen much before term.

(3) Histochemical Age Changes.

The histochemical age changes in the placenta have been studied by Wislocki and Dempsey (1946), and they have demonstrated distributions typical to various stages of pregnancy. Wislocki et al (1948) have demonstrated the main sources of hormones and suggested that the steroids are syncytial in origin and the gonadotrophins arise from the cytotrophoblast. Various authors, quoted by Reynolds (1949), found that in the postmature placenta the arginine content remains high as against the usual low level at term.

(4) Histological Changes in Disease.

In pre-eclampsia Tenney (1936) has demonstrated degeneration of the syncytial nuclei which is directly proportion-:al to the severity of the disease and in eclampsia states that

he found no normal syncytium. This work was confirmed by Tenney and Parker (1940) and they related the changes to the degree of albuminuria rather than to the height of the blood pressure. Wislocki et al (1948) found that the normal histo-:chemical changes of age were seen at a much earlier stage of pregnancy in pre-eclampsia. Zeek and Assali (1950) have stated that in pre-eclampsia there are degenerative changes in the blood vessels of the decidua. Gross changes of the placenta in the nature of "red infarctions" have been said to be more commonly seen in association with maternal pre-eclampsia (Young, 1914; Bartholomew and Kracke, 1932; Falkiner and Aphthorpe, 1944).

(5) Rate of Metabolism.

This is essentially a measure of the activity of its epithelial layers. This has been studied by Page (1948) and Hellman et al (1950). Both found a gradual fall in rate of metabolism in the last ten weeks of gestation. Page found a grossly decreased rate of metabolism in pre-eclampsia but Hellman et al could not confirm this. Both groups of investigators think that the fall in rate of metabolism can be fully explained by the epithelial degeneration which occurs with ageing as judged by the histological changes.

(6) Functional Studies of Placental Transfer.

These studies do not measure the efficacy of the placental membrane as an isolated factor but the total summation of the effect of all factors concerned; the concentration in the maternal blood, the placental blood flow, the characteristics of the membrane, and the demand by the foetus, are all factors in the final results. In late pregnancy, transfer of various easily diffusible substances has been studied.

Oxygen - the work of Barcroft et al (1934) in the goat, andBarcroft et al (1939) in the sheep, Barcroft and Young (1945) and Synder (1949) in the rabbit, has been discussed earlier.

Flexner and Gellhorn (1942) have studied the rate of transfer of sodium and water in most mammalian foetuses, and Flexner et al (1948) Hellman et al (1948),and Kaiser and Cushner (1951) more particularly in the human. It has been shown that the rate of transfer per unit weight of placenta increases throughout the first nine-tenths of pregnancy, but falls precipitously after that time. The rate is transfer is not influenced by normal labour, anaesthesia, or easy forceps delivery. The amount of sodium and water transferred at the 36th week is much greater than the foetal needs at that time, and even at term, though the rate is falling rapidly, transfer

is above the needs of the normal foetus. In pre-eclampsia the rate of transfer of sodium has been shown to be much reduced. Cox and Chalmers (1953) have found at term in the human similar rates of transfer of sodium to those of Flexner, and have confirmed that normal labour has no effect on sodium transfer. They found a decrease in the rate of transfer in pre-eclampsia and in one case showing foetal distress.

## (IV) FACTORS INFLUENCING THE UPTAKE OF OXYGEN BY THE FOETUS AND THE SUPPLY AVAILABLE TO INDIVIDUAL TISSUES.

### (1) Haemoglobin and Red Cells in the Foetus.

The ability of the foetal blood to take up and transport oxygen depends in the first instance on the amount of haemoglobin contained in each unit volume of blood. Little or no observations are available of the variations in the haemoglobin level of the blood of the human foetus throughout pregnancy and information from animal experiments, though extensive, is confusing, and not necessarily applicable to the human.

Wintrobe and Shumacker (1936) in small series of human foetuses showed evidence that the haemoglobin reached normal adult levels by the 23rd week (Fig. 15), and that the red cell levels rose steadily from the 76th to the 198th day.

More studies have been made of the cord blood of the infants immediately after birth and the results of a representative sample are seen in Table V.

In all investigations there is a wide scatter in both haemoglobin and red cell counts. The mean haemoglobin values vary from 15.36 to 17.90 g. per 100 ml. with extremes of 11.86 and 22 g. per 100 ml. The mean red cell count in the three series in which it is recorded does not vary much but in each

series there is a wide range of values with extremes of 3,300,000 to 6,000,000. No explanation has been offered of those wide variations.

The results of very many other investigations have been published which purport to study the haemoglobin levels and red cell counts of the infant at birth. Samples were, however, taken at varying times in the first two days of life, and blood was obtained from venous sinuses, or capillary vessels. Wegelius (1948) has shown that the haemoglobin and red cell levels begin to rise within the first half-hour of life and there is a steady change for at least the first two days. Oettinger and Mills (1949), amongst others, have shown that samples from capillary and venous blood give widely different readings. Any reading of haemoglobin and red cells which purports to define the levels at the moment of birth must therefore be made on cord blood and immediately on birth.

Variations in the haemoglobin and red cell levels throughout pregnancy have been studied in the cat by Windle (1940) and in the pig by Jones et al (1936). In both there is a rise in red cell count during pregnancy which continues after birth.

Wintrobe and Shumacker (1935, 1936) studied the haemoglobin and red cell levels of the blood during foetal life in the pig, rat, rabbit and dog. They concluded that on the whole there was a steady rise as pregnancy advanced. A scrutiny of their

results shows that the haemoglobin level has frequently reached normal adult levels by term but that the red cell count has not done so and is still rising. The levels reached at term vary somewhat with the stage of development reached at birth.

Barcroft (1946), however, in a study of blood of the foetal sheep, found that the haemoglobin levels rose fairly rapidly to the end of the first third of pregnancy (50th day) and then steadily but more gently till the 125th day, when they are about normal adult levels. In the last 15 days there is again a steep rise. (Fig. 7). The most striking feature, however, was the way in which, in the last 10 to 15 days of the gestation period, the points fan out so that at term the highest figure is about double the lowest, the rise above normal adult levels being seen in most but not all foetuses.

Barcroft et al (1939) and Barcroft (1946) attribute the rise in haemoglobin in the sheep above normal adult levels, (which might occur after the 125th day), to the active production of haemoglobin in response to the falling oxygen supply which might begin about that time. The wide variation in readings in the last 15 days can be explained by a varying degree of anoxia in the individual cases.

(2) Dissociation Curves of the Blood of the Foetus.

The affinity of blood for oxygen at a given partial pressure of the gas is represented by the dissociation curve.

The shape and position of the curve is influenced by two factors, (a) the chemical nature of the haemoglobin, and (b) the physical and chemical environment in which the haemoglobin finds itself, e.g. within or without the corpuscle and the temperature, hydrogen ion concentration, and salts.

Increased acidity causes aggregation of molecules of haemoglobin and alters the shape and position of the curve, and reduces the saturation with oxygen at any given pressure, i.e. "a shift to the right."

(a) The Nature of the Haemoglobin. Studies of the dissociation of the haemoglobin in the developmental phase of the bull frog (Mc Cutcheon, 1936), chick (Hall, 1935), rabbit (Hall, 1934) have been performed.

The dissociation curve under standard conditions is not the same throughout the developmental period. The change is always in the direction of a decreased affinity for oxygen as time progresses, and a tendency for a change from a hyperbolic to a sigmoid curve (See Figs. 16 and 17), but the haemoglobin of the foetus always has a greater affinity than that of its mother.

In man dissociation curves for foetal and maternal haemoglobin were determined by Hill (1935) (Fig. 18),

Haurowitz (1935), and McCarthy (1943). The most important finding is that, unlike all other species, foetal haemoglobin had a lower affinity for oxygen than that of the mother. This is the exact opposite to the behaviour of foetal and maternal corpuscles.

(b) Blood. Haselhorst and Stromberger (1930, 1931) showed that the bloods of the foetus and mother possessed different affinities for oxygen, and McCarthy (1943) (Fig. 19) has shown that while the difference is due to the haemoglobin itself, the direction of difference is due primarily to the properties of the maternal corpuscles, which cause a marked decrease in the oxygen affinity of haemoglobin. The foetal corpuscles have little effect on the affinity of their contained haemoglobin.

Extensive studies in the foetal and maternal blood of the cow (Roos and Romijin, 1938) (Fig. 9), the sheep (Barcroft, 1946) (Fig. 8), and the goat (Barcroft et al, 1934) (Fig. 20), have been made and the following general observations are made by Barcroft (1946).

The mechanism in the early phase of foetal life is particularly adapted for picking up oxygen from the mother at low pressures but not for saturating the foetal blood to the maximal extent. At the later part of foetal life the accent is the opposite. The foetal blood is less adapted than it was for picking up oxygen at low pressures but more adapted for

saturating itself at somewhat higher ones. The maternal curve is moved to the right of the normal non-pregnant adult and this tends to release oxygen at all pressures, but its sigmoid shape accentuates this tendency at low saturations and thus making up for the lesser efficiency of the foetal curve in this region.

In man, the dissociation curves of foetal and maternal blood have been studied by Haselhorst and Stromberger (1930, 1931), Noguchi (1937), Eastman et al (1933),(Fig. 21), who studied the relationship of foetuses born at term, and by Darling et al (1941), Leibson et al (1936), and Sachs and Likhnizkaya (1938), who studied the foetal maternal relationships in the later half of pregnancy.

The foetal curves are always to the left of the maternal under standard conditions of pH 7.4 at 37°C. but there is a smaller gap than in the ruminants. According to Darling et al (1941) the foetal and maternal curves have the same inflection, i.e. they are practically parallel. The maternal curve is well to the right of that for normal non-pregnant women. (Fig. 20).

Leibson et al (1936) and Sachs and Likhnizkaya's(1938) findings were almost the same as those of Darling et al (1941) for foetuses at or near term, but they showed that the curve for the foetal blood is variable up to the 35th week of pregnancy.

The dissociation curve in mid pregnancy was uniformly more inflected than that of adults or term foetuses (Fig. 22).

(3) The Haemoglobin in the Blood of the Foetus.

The different affinities for oxygen of foetal and adult haemoglobin, both within and without the cells, have been discussed (see page 36).

There are important differences in behaviour between human and animal haemoglobins and between foetal and adult haemoglobins. Human foetal haemoglobin has a lower affinity for oxygen than adult haemoglobin, and is more resistant to denaturation in strong alkaline solution. Those properties are the exact opposite of the the characters of other foetal haemoglobins. (Korber, 1866; Haurowitz, 1930 and 1935; Brinkman et al, 1933; Hill, 1935; McCarthy, 1943; Jonxis, 1949).

Other differences in human foetal and adult haemoglobin have been discovered and are detailed by Jope and O'Brien (1949).

(a) Proportions of Adult and Foetal Haemoglobin in the Blood of the Foetus. The content of adult haemoglobin in the blood of the human foetus, at term, has been studied by Brinkman et al (1933), Haurowitz (1935), Ponder and Levine (1949), and Zeisil (1951), by estimating the resistance to alkali denaturation, and by Beaven et al (1951) by studies of electrophoretic mobility, and the disappearance of foetal type haemoglobin after birth by the same investigators and by Jonxis (1949).

At birth the percentage of adult haemoglobin varies from 0 to 30 per cent. but is lower in premature infants. Beaven et al (1951) found 6 per cent. in one case at the 20th week. Foetal haemoglobin disappears from the blood of the infant by the 5th month, but takes longer in the infant prematurely born. The relationship between foetal/adult haemoglobin is a function of age from conception and not of time of birth.

The work of McCarthy (1943) and of Jonxis (1949) has shown that adult and foetal haemoglobin are contained in different corpuscles, but no information is available of site of manufacture in the body or of the type of cells containing adult haemoglobin.

(4) Demand of the Foetus for Oxygen.

The amount of oxygen required by the foetus will depend on its weight and the metabolic rate of the foetus as a whole.

(a) Oxygen used by the Foetus. Barcroft et al (1934b and 1939a) found that the sheep foetus used 4 c.c. of oxygen per kilo body weight per minute over the last quarter of gestation. Barcroft and Elsden (1946) put the figure, however, somewhat higher, at about 5.5 c.c. per kilo per minute.

Carlyle (1948) studied the oxygen uptake of individual foetal tissues. He estimated that there is uptake of oxygen at 4 c.c. per kilo per minute in the last quarter of gestation.

This is about half the amount taken up in the mid-pregnancy period. The fall is due to the fact that the tissues which make up the main weight of the foetus in later weeks have a low oxygen consumption (bone muscle, skin and blood), but others (brain, stomach, intestine and lung) increase oxygen requirements as they develop. The brain, for example, at or about birth has a very high oxygen requirement.

(b) Growth of the Foetus. The increase in crown rump length of the sheep foetus is a straight line from the 45th day onwards (Barcroft and Kennedy, 1939) but weight behaves differ-:ently. Barcroft (1945) has shown (Fig. 23) that in late pregnancy the weights fan out and at term a foetus may weigh anything from 2 to 7.7 kilos.

Scammon and Calkins (1929), Dunham (1948) and Thomson (1951) have provided similar information for the human foetus. Thomson (1951) provided some evidence that there is a slowing of the incremental growth in the human foetus near term, and Karn and Penrose (1951) (Fig. 24) showed that increase in weight ceased after the 295th day.

Thomson (1951), however, showed that in the human foetus there could also be a wide scatter of weights, from 4 to 10 lb. at term when the average weight was 7.23 lb.

Calkins (1937) showed that the foetal portion of the human placenta increases steadily in weight throughout pregnancy.

An investigation of foetal growth has been undertaken

undertaken in the Midwifery Department of the University of Aberdeen, and an abstract of results available to date is seen in Fig. 72. Increase in weight of foetus and placenta continues up to the 43rd week, but the amount of increase after the 41st week is very small. The incremental growth rate starts slowing about the 33rd week.

Summary and Conclusions. The total oxygen required by the foetus depends on its weight and on the metabolic activity of its individual tissues. It would appear that in the human the total demand for oxygen would increase steadily throughout pregnancy, although the increasing demand in each week after term would be slight. The total amount of oxygen demanded per minute by a small foetus should be much less than that needed by a larger foetus at the same stage of gestation.

The human placenta increases steadily in weight throughout pregnancy.

(5) The Foetal Circulation.

The path taken by the umbilical blood after it reaches the foetus and the relative proportions of this blood which ultimately reach the foetal brain will dictate the oxygen environment under which the foetus must live in utero. Changes in oxygen saturation of the umbilical vein blood would interfere with the supply to the brain, but so too would an alteration in the proportion of umbilical vein blood in the carotid vessels.

(a) The Foetal Circulation in the last few Weeks of Pregnancy. The detail of the circulation in the mature foetal sheep has been extensively studied by Barclay, Franklin and Prichard (1946), whose findings are summarised here.

Oxygenated blood from the placenta (60 per cent. saturated at term) passes in the cord in two veins which unite to form a single umbilical vein flowing to the liver. About one-ninth of the blood passes direct to the inferior vena cava in the ductus venosus; the rest forms an afferent supply (with a high nutrient and oxygen content) to the central and left thirds of the liver. The other third, the right mass, is supplied by the portal vein with blood low in nutrients and with probably high waste content.

Passage is rapid through the liver. The inferior vena cava thus receives blood from four sources.

(1) The ductus venosus (60 per cent. saturated with oxygen).

(2) From the lower abdomen and legs (10 per cent. saturated).

(3) The liver outflow of umbilical vein blood (less than 60 per cent. saturated).

(4) The liver outflow of portal vein blood (about 10 per cent. saturated).

The blood reaching the heart is thus much less than 60 per cent. saturated. On reaching the heart, the great mass of the blood passes direct to the left atrium through the foramen ovale and meets and mixes with the pulmonary return flow which must reduce the saturation still further. The combined bloods pass

then into the left ventricle to reach the aorta. Most passes to head, neck and forelimbs, but a little goes into the coronary vessels and a little over the arch of the aorta.

It will thus be seen that the liver, heart muscle and brain get blood with the highest oxygen saturation. By the time the blood reaches the brain, the oxygen saturation is, however, depleted by much admixture of other blood.

As pregnancy nears term, the growth of the hind-quarters of the foetus is relatively great and the amount of blood of low saturation (10 per cent) returning in the inferior vena cava increases. This has the effect of diluting even further the oxygen saturation of the blood reaching the heart and the carotid vessels. Barcroft et al (1938) and Barcroft and Kennedy (1939) have studied the relation between the umbilical vein blood, the carotid blood, and the blood of the cerebral venous sinuses in the sheep (Fig. 25). At term, when the blood in the umbilical vein is 65 per cent saturated, that in the carotid 50 per cent., and that in the sinuses 20 to 30 per cent. The oxygen tension in the bloods is 30, 25 and 15 mm. of mercury respectively.

Lind (1953) has studied the circulation in the human foetus. The blood in the umbilical vein is distributed very similarly to that in the sheep but a smaller amount passes through the liver (Fig. 26). The distribution within the heart, however, is similar (Figs. 26 and 27).

(b) Changes at or after birth. In late pregnancy the umbilical vein, ductus venosus and ductus arteriosus are easily stimulated to contract and the calibre is variable. (Barclay et al, 1946; Lind, 1953). Immediately on birth, adjustments take place. It is not known in what order all occur but it would appear that the mechanical stimulus of stretching or rupture of the cord causes the ductus venosus to close by sphincter action. The foramen ovale closes very quickly (Barcroft et al, 1937) due to the increase in pulmonary venous return following opening up of pulmonary circulation (Barclay et al, 1946). The ductus arteriosus closes at first by muscle action (after closure of the ductus venosus and of the foramen ovale). Closure of the ductus arteriosus follows establishment of an adequate pulmonary circulation and increased oxygen saturation of the blood passing through the ductus (Kennedy and Clark, 1942).

Lind (1953), in the human foetus, found a similar sphincteric closure of the ductus venosus and that normally within two hours of birth the foramen ovale and ductus arteriosus were functionally closed.

(c) Anomalies of closure of foetal vessels. Barclay et al (1946) in the sheep and Lind (1953) in the human have shown that if adequate pulmonary respiration and pulmonary flow

are not established, or the oxygen saturation of the blood does not rise, functional closure of the foramen ovale and ductus arteriosus may not occur. (Fig. 28). Where closure has been adequate those pathways may reopen, and the circulation revert to a foetal type, should conditions of respiration and pulmonary flow deteriorate.

## (V) FOETAL RESPONSE TO ANOXIA.

### (1) Haemoglobin and Red Blood Cells.

Barcroft (1946) has shown that there is a very close inverse correlation at term in the sheep foetus between the haemoglobin level and the per cent. saturation with oxygen of the blood in the umbilical artery. (Fig. 29). He considers that in response to a falling oxygen supply the sheep foetus produces more red cells in an attempt to maintain the oxygen content. The foetus can therefore combat a gradually falling oxygen supply to some extent by an increase in the oxygen carrying capacity of its blood. This response takes some little time to develop, and is not seen with acute anoxia. (Snyder, 1944, 1949).

### (2) Resistance to Anoxia.

Glass et al (1944) studied the survival term in nitrogen of rabbits, dogs and guinea pigs. They demonstrated that in rabbits, (Fig. 30), resistance to oxygen lack is high at the onset of viability (thirty times adult time) but falls thereafter. At term, it is twenty times adult time, and in the postmature is fifteen times adult time. Within 20 days the newborn rabbit's resistance becomes the same as the adult.

Resistance to anoxia is a function of age and not of time of birth as the rabbit foetus, three days postmature at birth, has the same resistance as a 3-day old rabbit born at term.

Resistance is allied to stage of development at birth and it therefore is different in different species. Dogs and rabbits are about the same stage of development at birth despite the widely different gestation periods, and dog and rabbit foetuses born at term survive oxygen lack for the same time (31 minutes). The guinea-pig with the same gestation period as the rabbit is much more fully developed at birth, and the guinea-pig foetus survives oxygen lack for only 6 minutes (twice adult time).

Brinkman (1953) considers that the human foetus can survive a total lack of oxygen for about 30 minutes, provided its circulation is intact, and lesser degrees of anoxia for longer periods. It is doubtful if it will always survive completely unharmed as the higher cerebral centres are less resistant than the lower centres directly concerned with survival.

Darke (1944) has concluded that significant mental retardation is highly probable in infants who are severely asphyxiated at birth, thus confirming the work of Lund (1941).

Helstrom and Jonsson (1953) studied 85 infants who had been asphyxiated at or shortly after birth. Eighteen died in the newborn period of cerebral haemorrhage, and four later. Of the remaining 63 cases, 61 were examined and 18 showed signs of permanent cerebral injury at follow up (spasticity, convulsions,

oligophrenia). Sixteen of the remainder showed abnormal electro-encephalograms but no clinical evidence of cerebral damage (d'Avignon and Keilson, 1953).

Himwich et al (1941) consider that the resistance of the newborn to anoxia is due to (a) a low cerebral metabolic rate, (b) poikilothermia, (c) a capacity for anaerobic metabolism. If the anaerobic use of blood sugar is denied to the foetal animal, the survival time under anoxia is no better than the adult. Brinkman (1953) confirmed those findings and suggested that survival time could be increased by maintaining a high level of blood sugar or by cooling the foetus.

Snyder and Geiling (1943) showed that when the rabbit foetus was born by Caesarean Section after the mother had received a moderately heavy dose of morphia, the narcotised foetuses had a greater resistance to anoxia than those normally born (Fig. 31). Respiration was, however, depressed.

(3) The gasp.

Much has been written and much argument has arisen about respiratory movement of the foetus in utero. Barcroft (1946) and Snyder (1949) summarise the discussion. It would appear that inhalation of amniotic sac contents deep into the lungs (as against a tidal flow in the larger air passages) depends on a reflex "gasp" by the foetus.

The "gasp", which is not a normal respiratory movement, is a very premature reflex, occurs only when the upper cerebral centres are depressed and inhibited by severe anoxia, and is a response of the lower medulla (Barcroft, 1946). If the foetus in the last trimester is subjected to severe anoxia in utero, it will "gasp" and will inhale deeply. Where the amniotic fluid is relatively clear of vernix or of meconium, the fluid so inhaled may be absorbed but if a great deal of particulate matter is present, as in late pregnancy, or if meconium has been passed, the smaller air passages may be blocked to the detriment of future respiratory function. (Cases 1 to 8). A gasping type of respiration during or immediately after birth is significant of anoxia of severe degree, and not part of the normal pattern of the onset of respiration.

## (VI) CLINICAL SYNDROMES ASSOCIATED WITH ANOXIA.

### (1) Stillbirth and Neonatal Death.

Analyses of autopsy findings in stillbirth and neonatal death have stressed the importance of anoxia as a primary or contributory cause. In a study of 530 stillborn foetuses, Morrison (1952) found anoxia to be the cause of death in 232 (43.8 per cent.), (26 per cent. of all antepartum and 55 per cent. of intrapartum deaths). From autopsy of 800 infants dying in the neonatal period, Cruickshank (1930) considered that anoxia was responsible for 67.5 per cent. and was an important contributory factor in deaths from other causes. In studies of mixed groups of stillbirths and neonatal deaths, Potter and Adair (1943) and McGregor (1946) found anoxia as a sole cause in 40 per cent.

(a) Clinical Cause of Anoxic Death of the Foetus. Anoxia is a non-specific lesion arising from diverse clinical syndromes. Morrison (1952) classified the causes of anoxic death in his cases as seen in Table VI. Antepartum haemorrhage is the common-:est cause. Eight per cent. of all stillborn foetuses die of anoxia due to difficult labour, and nearly 13 per cent. from anoxia without an obvious clinical cause, most of such unexplained deaths occurring during labour. Interference with cord circul-:ation accounts for most of the remaining anoxic deaths.

No clinical explanation was found for 30 per cent of all anoxic deaths.

(b) Anoxia in relation to Prolonged Pregnancy. Death during labour of the postmature foetus is commonly attributed to mechanical difficulty because of increased size of the foetus, excessive ossification of the head and ineffectual uterine contractions. De Lee and Greenhill (1947), although stressing the importance of these factors, state that "the child may die from no other apparent cause than being over-mature."

Clayton (1941) found that when pregnancy lasted 42 weeks or more there was, in infants over 7½ lb., an excess of stillbirths over infants born at term. He considered that the excess mortality was due entirely to difficult or prolonged labour. Rathburn (1943), Latto (1951) and Clayton (1953) confirmed these findings. McKiddie (1949), however, found that the increase in the stillbirth rate was due mainly to an increase in deaths, clinically unexplained, and suggested that a falling oxygen supply to the foetus might be the most important primary cause.

Gibberd (1952) confirmed findings of previous authors but studied the autopsy findings in addition to the clinical features. He found that the excess stillbirth rate after term was due to an increase in anoxic deaths without demonstrable clinical reasons for the anoxia. He found also an increase after term in neonatal deaths from anoxia.

(2) Foetal Distress.

The significance of foetal heart irregularity or slowing as a sign of anoxia has been discussed by very many authors from Naegele (1838) to Mayer (1953). An excellent review and description of the problem is that by Lund (1940; 1941) who investigated the aetiology of foetal distress in 2000 consecutive deliveries. From a classification of the state of the infant at birth he estimated the incidence of "asphyxia" to be 18.9 per cent. in primigravidae and 11.7 per cent. in multigravidae. The incidence of asphyxia at birth was much higher if the pregnancy was complicated by pre-eclampsia, contracted pelvis or maternal diabetes. He also considered that asphyxia at birth was more likely after labours lasting under 4 hours or over 30 hours.

He considered that anoxia in utero was manifest by a slowing of the foetal heart sounds and that acceleration did not occur. In his series, 40 per cent. of infants showing foetal heart slowing in labour were asphyxiated at birth, and 30 per cent. where the passage of meconium had been the only sign of distress.

McKiddie (1949) was the first to demonstrate an increase in incidence of "foetal distress" during labour after the 41st week of pregnancy and that the incidence rose with the degree of postmaturity. The postmature foetus was, however, not more

likely to show asphyxia at birth.

(a) Clinical Significance of Passage of Meconium by the Foetus. Knappe (1897) presents a historical review of the subject. Before the recognition of the foetal heart the passage of meconium had been considered a sign of foetal death. In the time of de la Motte (1655-1737) some authorities considered the passage of meconium as a sign of death, others only that there was a danger of death. De la Motte discussed the importance in various presentations and considered that in prolonged labour, or with prolapse of the cord, it was of serious significance. Schwarz (1858) considered that the appearance of meconium was a sign of the suppression of respiratory interchange, and that meconium as a sign of asphyxia preceded foetal heart slowing and distinguished two types of asphyxia. In the first, meconium was passed; in the second, the foetal heart slowed.

Schulze (1925) found that the incidence of meconium in the liquor was usually understated, especially in short labours. He also noted that very large infants were more likely to pass meconium in labour, and concluded that the passage of meconium was not a sign of foetal asphyxia unless accompanied by slowing or irregularity of the foetal heart. Similar conclusions were reached by Freed (1927).

It is stated in most text-books that the passage of meconium is due to relaxation of the anal sphincter consequent on severe anoxia. Clinical and autopsy evidence, however, shows that when a foetus is severely anoxic, it will empty its colon from the caecum and pass large amounts of meconium. This ability would indicate active peristaltic action. All experimental work on the adult colon shows that activity is depressed by anoxia (Van Liere, 1942) although diarrhoea with the passage of bile is not uncommon at extreme altitudes. (Barcroft, 1925).

Noguchi (1937) suggests that passage of meconium in the foetus is due to an increase in carbon dioxide tension consequent on a lowering of the pH of the blood. The blood of the anoxic foetus certainly has a very low pH secondary to the excess production of lactic acid, (Eastman and McLane, 1930; Eastman, 1932), but this excess is probably seen only in association with the anaerobic metabolism of glucose. Windle and Bishop (1939) found that active peristalsis of the gut in the newborn kitten which was still active when the blood was 40 per cent. saturated with oxygen, stopped when the blood was only 12 per cent. saturated.

Becker et al (1940) in a study of the guinea pig foetus, showed that the amniotic sac contents were normally swallowed and passed along the gut by active peristalsis. If the mother

was made anoxic, swallowing was more active but peristalsis was impaired. Late in foetal life meconium was frequently passed and re-swallowed. Results on the guinea-pig must be applied with caution to the human. The guinea-pig is born much more developed than the human foetus at term (it forages for food immediately). In addition, we have seen that it is much less resistant to anoxia (see page 47 ). The passage of meconium by the foetal guinea-pig probably, therefore, indicates that the oxygen supply is falling rapidly in late pregnancy and that the foetus with a brain metabolically very active is poorly equipped to resist even moderate anoxia.

(3) Summary.

(a) Anoxia is a frequent cause of stillbirth and neonatal death and in about one third of cases is clinically unexplained (see Table VI). "Unexplained" anoxia is more frequent when death occurs during labour.

(b) The increase in the stillbirth rate which occurs after the 40th week of pregnancy is due to an increase in death from "unexplained anoxia." Some authors, however, consider that death due to difficult labour is the main cause of the increased rate after term.

(c) Slowing or irregularity of the foetal heart is a more accurate prognostic sign of "asphyxia" at birth than is the presence of meconium. (Asphyxia is a clinical state and

in many cases is due, not to anoxia, but to cerebral birth trauma).

(d) Some investigators consider that meconium is a sign of anoxia in utero and precedes foetal heart signs if anoxia alone is present.

(e) The passage of meconium is due to stimulation of the gut by an alteration in carbon dioxide tension in the acid blood of the anoxic foetus.

(f) Results in animals are not necessarily applicable to the human.

## METHODS AND TECHNIQUES.

A description of the laboratory techniques used,
and the selection and classification
of clinical material for study.

---

## (I) ESTIMATION OF HAEMOGLOBIN.

Before beginning the estimation of haemoglobin, the methods available were reviewed. The essentials for this investigation were accuracy, ease of estimation, and a method applicable to small quantities of blood.

Iron analysis was not further considered because of the technical difficulty of the methods, and gaseous methods of estimating oxygen capacity for the same reasons as discussed later under "Estimation of Oxygen Content."

Clinical methods in common use were considered and discarded in the light of the work of Macfarlane et al (1948) and a photometric method was chosen in preference to calori-:metric methods in view of the work of Macfarlane et al (1948) and King et al (1948a). The method finally used was photometric and the instrument the Grey Wedge Photometer (King et al, 1948b).

This instrument, described originally by King,(1947) is a modification of previous Grey Wedge photometers and is commercially produced as the "M.R.C. Grey Wedge Photometer."

### (1) The M.R.C. Grey Wedge Photometer.

The commercial instrument was tested by King et al (1948b), who found that the results, in the hands of eight observers, were of satisfactory reliability and no one of 240

estimations was more than 5 per cent. Haldane from the true value (as estimated by iron analysis and analysis of oxygen capacity). The standard of accuracy was higher than that found with all methods other than base-line methods, (i.e. iron and oxygen capacity).

(a) The Instrument. The instrument used was calibrated by the National Physical Laboratory and certified to be accurate to within 3 per cent. over the range of haemoglobin readings 50 to 150 per cent. The instrument is calibrated so that "100 per cent." equals 14.8 gm. Haemoglobin per 100 c.c. blood. Since it is a photometric instrument, it measures optical density of the coloured solutions and the light absorbed is balanced by rotating an annular grey wedge until equal brightness is obtained in both halves of the field. A match is made possible by the fitting of a monochromatic light filter (Ilford bright spectrum yellow green No. 625) over the eye-piece. The end point may be approached from dark or light sides, and by rotating the wedge about the end point a very accurate match can be obtained.

(b) The Technique in Use. The technique is simple in use and details can be found in original publications, but possible errors in haemoglobin estimations in general and with this instrument in particular must be considered and avoided.

Sampling errors in obtaining capillary blood were avoided, since all samples were taken of cord blood available freely and in reasonable amounts. Blood samples were taken in small test tubes with dried Wintrobe solution as an anticoagulant. Before pipetting blood for analysis the test tube contents were mixed to avoid false readings due to red cell sedimentation. Care was taken to mix blood with anticoagulant immediately on taking and estimations were done as soon as possible. It was found that if samples stood over-night, false high readings were occasionally obtained. Glass cells were washed and oven dried after each estimation, care was taken to ensure that the optical faces were clear, and cells were always handled by their side walls. If solutions are cold, a condensation mist forms and gives a false high reading. This is obvious, as the readings keep on rising. In view of the variability of daylight and since many estimations were performed during hours of darkness, the instrument was always used with its permanent in-built light source.

Readings were performed in triplicate and often from separate blood samples. The range of readings was never more than 2 per cent. and readings were averaged.

## (II) ESTIMATION OF OXYGEN CAPACITY AND PERCENT. SATURATION WITH OXYGEN.

The oxygen capacity of the blood was calculated on the basis that 1 g. of haemoglobin when fully saturated is combined with 1.34 c.cm. of oxygen. From the calculated capacity and observed content, the percent. saturation of each blood sample was obtained.

## (III) ESTIMATION OF RED CELL COUNTS.

Red cell estimations quoted here were performed by Dr. Elizabeth Turnbull, using a Neubauer counting chamber. The mean of four counts was taken but in every case the four counts were within a total range of 200,000.

## (IV) ESTIMATIONS OF PROPORTIONS OF FOETAL/ADULT HAEMOGLOBIN.

The estimations quoted here were performed by Dr. Elizabeth Turnbull. The varying resistance of adult and foetal haemoglobin to denaturation by alkali was used to demonstrate the proportionate contents in the blood sample. The technique was that described by Jonxis (1952) and is a modification of that of Brinkman and Jonxis (1937).

## (V) ESTIMATION OF OXYGEN CONTENT.

Methods considered were:-

Gas extraction methods (Haldane, 1920; Van Slyke and Neill, 1924; Roughton and Scholander, 1943), Spectroscopic methods (Drabkin and Austen, 1936), Oximetric methods with cuvette samples (Brinkman and Wildschut, 1938; Wood et al, 1948; Wood, 1950).

The oximetric methods were discarded because, at the time, the necessary apparatus would not be easily obtained or built. Later study of those techniques showed that their accuracy is doubtful in the range of readings likely to be encountered in foetal blood where the per cent saturation, especially in arterial samples, may be well below 20 per cent. Those methods have the great advantage, however, that satisfactory readings can be obtained even with the presence in the blood of mixtures of anaesthetic gases.

Spectroscopic techniques were not freely available, chiefly because of the problem of obtaining the apparatus (Beckman precision spectrophotometer). The technical difficulty of filling a thin cell (0.007 cm.) with blood under anaerobic conditions is another practical drawback to the method. The accuracy is doubtful if nitrous oxide gas is present in the blood as other haem pigments may be formed.

The method of Haldane demanded moderately large blood samples (2 to 4 c.c.) for accuracy and for duplicate readings, and this amount of blood is not usually available from all foetal vessels.

The manometric method of Van Slyke and Neill has many advantages. It is, in trained hands, the most accurate method, and can be done with 0.2 c.c. blood, but its disadvantages under the circumstances of the present investigation were great. First, samples had to be obtained at the birth of the child, at any time, day or night, and analysed as soon as possible. The demands of heavy clinical duties meant that the time available for the work was limited and irregular. Manometric apparatus does not lend itself to infrequent and irregular use, and each experiment would have necessitated complete overhaul and adjustment. Estimations were sometimes made at the rate of two per day, but were often many days apart.

(1) The Micro-Technique of Roughton and Scholander (1943).

The micro method of Roughton and Scholander (1943) was ideally suited for the investigation. It is not a difficult technique once facility in handling the apparatus is obtained. It is ideally suited to occasional use and, apart from thrice-weekly preparation of fresh ferricyanide solution, requires no previous preparation. Investigation of very small samples is possible (as, for example, are obtained from the umbilical arteries of a 20-week foetus).

The accuracy of the method is limited by the visual ability of the operator to read fractions of the scale. Readings are probably correct to 0.1 to 0.25 vols. per cent.

The main disadvantage of the method is that it is not applicable to blood containing ether, and it is also very doubtful if it can be applied to blood containing nitrous oxide or other gaseous anaesthetics. (Roughton, 1952). In all cases investigated by this technique, therefore, the delivery was undertaken with spinal or local analgesia, or, on occasion, without analgesia.

(a) The Principle of the Method. The oxygen, carbon monoxide and nitrogen of the blood and reagents are extracted by an excess of carbon dioxide. The carbon dioxide is then absorbed with 10 percent. sodium hydroxide. The residual gas bubble is driven into the capillary (see Fig. 40) and its volume measured before and after absorption with alkaline pyrogallol. The difference in those two readings represents the oxygen content of the blood of the reagents. A blank run is made with reagents alone to measure the oxygen content of the reagents and this figure is subtracted from the oxygen content of the blood and reagents. The remaining reading, when multiplied by the usual correction factor for temperature and pressure, is the oxygen content of the blood sample.

(b) Practical Problems in Technique. (See Figs. 35 to 41). The bubble must be moved slowly and evenly to allow good drainage in the capillary and to match the conditions under which calibration was performed. The plunger is best moved with a screwing motion and a finger as a brake allows control of the plunger and prevents accidental movements (Fig. 40).

The main difficulties in the technique occur when filling the syringe from the pipette, and in maintaining atmospheric pressure in the syringe during extraction of the gas. The first can be overcome by grinding in the tip of each pipette to the syringe cup with carborundum powder so that a perfect glass-to-glass join is obtained.

The pipette and syringe should be held in the hands for the filling process (Fig. 37). The plunger is drawn back with the tip of the little finger, the clip being off. Once a perfect glass-to-glass junction is obtained, and after practice, no visible caprylic alcohol is drawn in with the blood sample.

When extraction of gases is taking place, the syringe is best shaken in the horizontal position but in a vertical direction, (Fig. 38). The clip should be off, and provided the syringe plunger has been adequately wetted with ferricyanide solution, it will be forced back by the developing gas. The pressure needs to be adjusted with care when the syringe is returned to the

vertical position, and the finger is removed from the top.

The residual bubble should be moved into the capillary just before complete absorption of carbon dioxide has taken place and final absorption completed in the capillary as the partial pressure of oxygen is high in the bubble and low in the sodium hydroxide in the syringe and the bubble may lose oxygen to the hydroxide if left too long in contact. Absorption of oxygen by pyrogallol can be achieved by drawing the solution down into the capillary but with long bubbles this means that the bottom of the gas bubble is drawn into the hydroxide in the syringe. Alternatively, the gas bubble may be driven into the pyrogallol in the cup, with the syringe inverted and then sucked back once absorption has occurred.

Equilibration at a fixed temperature is necessary as with long bubbles a difference of at least one division is found at 20°C. (Fig. 41).

Initially three readings were made, and results averaged, and it was seen found with practice that individual readings were within a total range of 0.5 vols. per cent. and in most of the investigation quoted, two (or occasionally three) readings were performed. Very occasionally with samples from umbilical arteries blood was available for only one reading.

(With the technique of collection of blood and filling of syringes used, an initial sample of at least 1 c.c. of blood was necessary for two readings, as there is always blood lost, when

sealing the collecting syringe initially (Fig. 33), and on each occasion after filling the pipette).

(c) Accuracy of the Method. According to the authors, the blood can be analysed up to 24 hours after taking, provided it has been stored in ice water. In a few instances in this series, it was found impossible to test samples before 6 hours after taking, but in the big majority of instances, samples were tested much sooner. A few test runs were made of samples at 2 and 12 hours to test the validity of results obtained up to that period and no loss or gain of oxygen was noted.

The authors of the technique have tested the method by analysis of atmospheric air for oxygen with an accuracy equal to the visual readings of bubbles. I carried out a similar test with my apparatus and similar results were obtained. (Table VII). Further tests carried out by the authors have established a similar standard of accuracy. Tested against the standard procedure of Van Slyke and Neill (1924), the authors found that the accuracy of the method was within 0.1 to 0.15 vols. per cent. for each reading. I have tested the technique in my hands against the Van Slyke manometer apparatus as used by an experienced operator, and have found similar correlation.

## VI. TAKING, TRANSPORT AND STORAGE OF BLOOD SAMPLES.

The technique of obtaining samples as described by Huggett (1927) in goats and by Barcroft et al (1939) for use in sheep, is not applicable to the human. Eastman (1930) obtained samples by extracting the umbilical cord through an incision in the uterus and sampling the cord blood with the foetus still in utero. This technique is not possible in most cases as the umbilical cord is not easily reached when a lower segment Caesarean Section is performed. An attempt to extract the cord in front of the presenting part would necessitate pulling and would interfere with cord circulation. It would not be without danger to the child.

It was felt that a technique should be developed which would be applicable to all cases and which would therefore allow results to be compared with each other. (The technique is similar to that described by Haselhorst and Stromberger, 1930).

### (1) Obtaining Samples.

As soon as the child is fully delivered, either from the lower segment or from the vagina, the umbilical cord is doubly clamped in two places about 8 to 10 inches apart. The outer clamps are applied simultaneously and the inner pair after-:wards. If the outer pair cannot be put on each at the same time, that nearest the placenta is put on first to ensure adequate filling of the arteries. A segment of the cord is thus obtained with the vessels distended with blood. Samples were taken immediately from the cord vessels into previously prepared

syringes, as described by Roughton and Scholander (1938). About 2 c.c. can usually be obtained from each umbilical artery, and 5 to 10 c.c. from the umbilical vein in the full term foetus. In very early foetuses and in infants with short thin cords, much smaller amounts may be obtained. (Fig. 32).

Even in tiny foetuses at 10 to 12 weeks gestation, samples could be obtained from the cord vessels for haemoglobin analysis, and at 18 to 20 weeks for oxygen levels. In the non-viable foetus, samples for oxygen analysis were obtained while the cord blood was still flowing immediately the infant was delivered.

An attempt was made to obtain blood as follows:-

Umbilical vein:- 3 c.c. for oxygen analysis (heparinised), 1-2 c.c. for haemoglobin, red cell and haematocrit (Dried Wintrobe Solution), 1 c.c. for adult/foetal haemoglobin measure-:ments (heparinised); Artery:- 2 c.c. for oxygen analysis (heparinised); Maternal vein:- 1 c.c. for haemoglobin estimat-:ions.

Where the blood in the segment of the cord was not sufficient to supply these amounts, extra quantities could be obtained for estimations other than oxygen analysis from the vessels of the placental end of the cord, preferably before delivery of the placenta. It was not feasible to leave the cord for any length of time, or store it in ice water, as alteration in oxygen content occurred and the blood would clot. The samples had to be withdrawn

within a few minutes. All samples were obtained by syringe and never by allowing the cord to bleed into a vessel.

(2) Preparation of Syringes.

All glass syringes were used, of 2, 3 and 5 c.c. capacity. Luer fittings were found the most convenient and each syringe was examined to ensure that the bore of the nozzle would not admit the tip of the Roughton and Scholander pipette to ensure a good glass-to- glass union so that the pipette could be filled without contact with air.

The syringes were well washed with soap and water and ether, and oven dried and then were made up in batches sufficient for one case. Each syringe was labelled with a coloured thread to indicate its use for foetal vein or artery or maternal vein. Syringes were then sterilised by autoclaving as it was often best to remove samples at the operation itself, and sterile equipment was necessary.

In the operating theatre or labour ward, the syringes were tipped on to a sterile towel. The plungers were lubricated with sterile vaseline. A little heparin solution was drawn into the syringe and the barrel wetted. The heparin was then expelled and the needle and nozzle left full of heparin, the syringe being freed of air bubbles by tapping or rotating. The blood vessels were punctured and blood smoothly aspirated. (Fig. 32). Care was taken not to fill syringes to full capacity, otherwise back leakage of air might occur. A small air bubble usually came in

from the needle and that was expelled. A little mercury was then pulled into the syringe. A half-inch length of catheter tube (16 French) was applied to the nozzle and filled with blood, by inverting the syringe and gently pushing the plunger. A small glass rod was then pushed into the rubber, keeping up the pressure in the plunger so that blood escaped past the rod as it was pushed home. (Fig. 33). No air was trapped by this method. The syringes were then completely immersed in ice water in a thermos flask for transfer to the laboratory. If they had to be left for more than one hour, the thermos was stored in the refrigerator.

## (VII) ESTIMATION OF DURATION OF PREGNANCY.

Methods of estimation of foetal age are many and varied, and each method has a sphere of usefulness.

Crown-rump lengths are most accurate in early foetuses and crown-heel in later months, and both are more accurate than foetal weight. In the human, however, conception age is rarely known and even coital age may vary within wide limits. Any method of estimation of age by length or weight must in the first instance be standardised against conception or coital age, so in the human, ages accurate to a few days may be available only in a few highly selected cases. As has been discussed earlier, the scatter in both weight and length is comparatively wide, especially in the last few weeks of pregnancy in mammals. In a clinically normal pregnancy, a foetus of 49 to 51 cm. crown-heel length and 7 to 8½ lb. in weight may be born at any time from the 37th to the 43rd week of gestation.

This thesis is concerned with the oxygen supply to the human foetus in the later half of pregnancy and estimation of duration of pregnancy in the cases concerned is essential to the accuracy of the results.

Since 1948, the duration of pregnancy (as calculated from the date of the last menstrual period) has been very carefully assessed in all deliveries in the Aberdeen Maternity Hospital.

At the patient's first visit to the ante natal clinic (usually before the 12th week), a careful menstrual history is taken and the date of the onset of the last period noted.

Throughout pregnancy, the height of the fundus, the onset of quickening, and the changes in maternal weight are recorded. The menstrual age at delivery is calculated, using a disc calculator (Thomson, 1949). The case notes are scrutinised by the consultant responsible, and all possible information is correlated. Where the "dates" are doubtful or obviously wrong, the case is classified as "duration uncertain" and this applies to some 13 per cent of all cases (Table VIII). In all cases of the oxygen series, the data were personally scrutinised and in any case of doubt the case was discarded. The main difficulties arose in pregnancies purporting to last more than 44 weeks.

Gibson and McKeown (1950) suggest that 1.42 per cent of human pregnancies may last more than 44 weeks. Stewart (1952b) has analysed very carefully a small series estimating the duration of pregnancy from known ovulation time. He considers that the maximum intercourse-delivery interval is 285 days, i.e. about 44 weeks menstrual age. A careful study of information available from many thousands of cases, as described above, suggests on clinical grounds alone that Gibson and McKeown's figures are suspect and that Stewart's opinions are most certainly true. Gibson and McKeown obtained records from hospitals, health visitors, midwives, etc. and experience has shown that if such information is not carefully sifted and scrutinised, it can be highly inaccurate. The reasons are many, but as an example, we have noted that in cases with pre-nuptial conception and in unmarried mothers, the "dates" are often well out. McKeown and Gibson (1952) on scrutiny, considered that in 60 per cent. of the cases which purported to last over 44 weeks, the menstrual history was inaccurate.

## (VIII) SELECTION AND CLASSIFICATION OF CASES.

### (1) Selection.

For the first period of the investigation no selection of cases was made except that oxygen estimation could not be performed where inhalation anaesthesia had been used. As many cases as possible were studied to obtain a picture of the oxygen levels at the moment of delivery. It soon became obvious, however, that only a very limited number of oxygen analyses could be obtained in normal pregnancy before the onset of labour. The haemoglobin levels (oxygen capacity) in the cord blood of the foetus and later the red cell levels were studied in as many cases as possible.

Blood was obtained from live foetuses delivered from the 12th week, so that the maturation pattern of the red cells could be studied. In those early cases, termination of pregnancy was by abdominal operation and had been considered necessary after consultation with the relevant clinical colleagues. Many termin-:ations were on psychiatric grounds and others had a history of recent, though healed, tuberculosis or serious medical disorder likely to have been aggravated by continuation of the pregnancy, but not manifest at the time of operation, and so would be unlikely to have interfered with the foetus. At the time of sampling the foetus was alive. No samples were taken from aborted foetuses.

It must be realised that there can very rarely be a reason for operative delivery of a foetus from a normal pregnancy in the period from the 22nd to the 36th weeks, and also that most infants delivered during that period must be from abnormal pregnancies. A few haemoglobin readings were obtained, however, from pregnancies considered normal. The two readings of oxygen contents at 29th and 30th weeks were obtained from normal foetuses where hysterotomy was performed as a preliminary to radical hysterectomy from early carcinoma of the cervix. A third such case at the 26th week was lost to the normal range - the haemo-:globin level was 60 per cent., the foetus having erythroblastosis.

Specimens obtained after the 36th week for <u>haemoglobin and red cell estimations</u> were taken from infants without regard for the method of delivery, anaesthesia or analgesia, but the "dates" were carefully assessed and the clinical factors of the case carefully noted.

(2) <u>Classification of Cases</u>.

Clinical histories were reviewed in all cases and primary classification was made.

Where, however, some cases appeared to give a haemoglobin or oxygen result outwith the expected group pattern, the clinical findings were carefully reviewed. In this way, two unexpected groups were isolated - for example, where the patient had lost her immediately preceding infant from stillbirth or early neonatal

death the oxygen and haemoglobin readings were outwith the expected pattern, even though the current pregnancy was clinically normal. Secondly, Dr. Turnbull noticed that where abortion had threatened early in the pregnancy, the haemoglobin levels at subsequent delivery were very much higher than the normal.

Once those two further groups were noted, all subsequent estimations fitted into group patterns.

Groups are as far as possible exclusive, except for the cases in the oxygen series where meconium staining was studied. In those the experiment was designed to test the oxygen levels where meconium staining was evident and factors likely to have reduced the oxygen supply below normal (e.g. pre-eclampsia or threatened abortion early in the pregnancy) were not excluded.

(a) Normal. The pregnancy is clinically normal. There was in particular no evidence of pre-eclampsia, or bleeding early or late. In the oxygen series, cases are subdivided into groups, before labour, after easy spontaneous delivery, and after prolonged or difficult labour.

In the haemoglobin and red cell series, labour was ignored as it did not appear to influence the haemoglobin readings.

(b) Pre-eclampsia. Cases are so classified where hypertension with albuminuria and/or oedema arises in the course of a pregnancy, where the blood pressure was previously normal.

(Hypertension and oedema or albuminuria associated with anaemia, cardiac disease, or nephritis, are of course excluded). "Severe" pre-eclampsia are those cases where more than 2 parts per thousand of albumen (Esbach scale) were found in a catheter specimen of urine. "Mild" cases are those without albuminuria or with less than 0.25 parts per thousand. All others are "moderate".

(c) Previous Stillbirth or early Neonatal Death. Elective Caesarean Section is frequently performed where the mother has lost her previous child by late abortion, stillbirth or neonatally, usually from anoxia or cerebral birth trauma. Opportunity was taken to study haemoglobin and oxygen levels in those cases. These were found to be outwith the normal range even though the current pregnancy was normal.

(d) Foetal Distress. Foetal distress is defined on clinical grounds as irregularity of the foetal heart or slowing to or below 100 beats per minute, or the passage of meconium in presentations other than breech.

This group was first isolated by the oxygen findings in cases showing recent meconium staining.

The writer wished to study this group separately. In the haemoglobin series, all cases showing distress are taken together, but in the oxygen series only those where meconium was passed have been studied.

(e) Threatened Abortion. The patient had been confined to bed for some days earlier in the pregnancy with vaginal bleeding which may or may not have recurred. Incidental causes of bleeding were excluded clinically. When at delivery, usually by Caesarean Section, placenta praevia was proven, the case is classified under that group.

## (IX) OBSTETRIC DEATH.

A research team in the Midwifery Department has devised a clinical classification of stillbirth and first week neonatal deaths studied together under the heading of "Obstetric Death." This classification is based on a careful study of the clinical factors of the case and the postmortem findings. The idea of the classification is to ascribe the death to the clinical factor primarily responsible. The classification is in the course of publication (Baird and Walker, 1954; Baird, Walker and Thomson, 1954).

### (1) Classification.

Obstetric deaths are classified into the following nine groups:- (a) Mature unexplained, (b) Anoxia under stress, (c) Trauma, (d) Pre-eclampsia or eclampsia, (e) Premature unexplained, (f) Antepartum haemorrhage, (g) Maternal disease, (h) Foetal deformity, (i) Other causes (infection, Rh incompat-:ibility, etc.)

Most groups are not relevant to the subject of this thesis, but the detailed clinical description of the features of the relevant groups is given.

(a) Mature Unexplained (M.U.). Cases in which death of a mature and "normal" infant occurs without any previous abnormality of pregnancy, and without more stress than that

experienced in normal labour. A birth weight of more than 5½ lb. is used to define maturity.

The assumption is that there must have been some failure in placental or foetal physiology, and as a result the foetus count not withstand the ordinary hazards of pregnancy and labour. Intra uterine death may occur before the onset of labour, and in some such cases maceration may mask postmortem pathology. The foetal heart sounds may disappear early in labour, or later during a short and easy labour, and at postmortem the lesions of anoxia are found, though there had been no evidence of a clinical cause for the anoxia. Or foetal distress without clinical cause may occur during a normal labour, and the infant dies shortly after birth from respiratory failure associated with inhalation of amniotic fluid and meconium, with or without superimposed pneumonia. (See Cases 1, 2, 3, 5, and 10 as examples).

(b) Anoxia under Stress (StrA). In reviewing cases, it was found that "unexplained" anoxic death sometimes occurred during or after prolonged labour (more than 36 hours) usually in association with uterine dysfunction, but without disproportion or cord abnormalities. (See Cases 6 and 7).

(c) Trauma (Tr.). This group defines those cases in which a healthy child has been killed by mechanical stress during labour or delivery (See Case 8). The decision to classify a death as traumatic depends not only on autopsy evidence of

birth trauma but also on the clinical characteristics of the labour and the degree of head moulding.

The group includes all foetal death associated with breech, shoulder, or other malpresentations, and all those associated with cord obstruction, as those causes of death are essentially mechanical. (See Case 9).

The group can be subdivided, however, into traumatic deaths due to difficult vertex delivery (Tr.Vertex) and all others (breech, cord, etc.)

(d) Difficult Labour. To study the obstetric death rate due to mechanically difficult or prolonged labour with the vertex presenting, deaths due to "difficult vertex delivery" and "anoxia understress" are combined. (Tr. Vertex and StrA). (See Cases 6, 7 and 8).

(e) Toxaemia (Tox.) Death occurs in the course of eclampsia or of severe or moderate pre-eclampsia; or neonatally, in such a case, and the toxaemia is considered primarily responsible. This category includes cases of accidental haemorrhage occurring in association with pre-eclampsia.

(2) Material Used.

A study was made of all stillbirths and first week neonatal deaths (931 obstetric deaths) occurring in 10785 primigravidae and 12723 multigravidae, cared for antenatally and delivered by the staff of the Aberdeen Maternity Hospital between the years 1938 and 1951 inclusive. For certain analyses, booked

cases delivered since 1948 only have been studied as the information available is more complete. After classification of the death, the influence of many different factors was considered. The influence of parity, maternal age, and length of gestation will be discussed in this thesis.

## (X) FOETAL DISTRESS.

Foetal distress has been defined as irregularity of the foetal heart or slowing of the heart rate with or without irregularity of rate or rhythm to or below 100 beats per minute, or the passage of meconium in presentations other than breech.

### (1) Material Used.

Cases of "foetal distress" occurring in 3504 "booked" primigravidae and 5312 multigravidae delivered in the Aberdeen Maternity Hospital in the four years from 1948 to 1951 were individually studied. After careful appraisal of the case notes, the "distress" was classified.

### (2) Classification.

(a) Type. "Heart" - where heart signs were present alone.

"Meconium" - where there was evidence that the foetus had passed meconium whether heart signs were also present or not.

(b) Cause. The following cause groups were defined:-

(i) Prolonged Labour. Where distress appears during the course of a prolonged labour and where there is no clinical evidence of disproportion. (See Cases 6 and 7 as examples).

(ii) Pressure. Where distress appears coincident with a period of pressure on the foetal head in its passage through the pelvis or when progress is halted by malposition. (See Case 12).

(iii) Cord. Where pressure on the umbilical cord, prolapse of the cord, or entanglement of the cord round neck or limbs appear to have been responsible. (See Case 9 as example).

(iv) Other. Distress in association with other factors, e.g. pre-eclampsia, antepartum haemorrhage, etc. (See Case 14 as example).

(v) Second Stage: Where in the late second stage there is a sudden drop in the foetal heart rate with the foetal head in the pelvic outlet. This very common group appears to be aetiologically separate. (See Case 13).

(vi) Unknown. Where there was no clinical abnormality of the pregnancy or labour which might explain why distress should have occurred. (See Cases 1, 2, 3, 5, and 11 as examples).

(3) Analysis.

Once the cases of distress were reviewed and type and cause designated, the effects of type of labour, maternal age, duration of pregnancy, and parity were considered.

## RESULTS.

Haemoglobin levels and red cell counts, and oxygen levels, in the vessels of the umbilical cord under normal and abnormal conditions of pregnancy and labour.

A statistical analysis of "obstetric death" and "foetal distress" and a short analysis of the incidence of "difficult" labour.

---

## (I) HAEMOGLOBIN AND RED CELLS.

### (1) In Normal Pregnancy.

In Fig. 42 the haemoglobin levels are seen in 145 cases in which there was no clinical abnormality in pregnancy or labour likely to have affected the foetal blood. The haemoglobin level is seen to rise steadily from 9 g. at the 10th week to reach 14 to 15 g. by the 22nd to 24th week. From the 36th week there is a general tendency for the level to rise but the results fan out so that by the 40th week, although the mean value is 16.5 g. the range is from 15 to 18.6 g. If the pregnancy should be prolonged, the rise is maintained and by the 43rd week the mean value is 18.8 g., the range,however, is from 16.8 g. to 20.5 g. A haemoglobin reading under 16.5 g. is rarely found after the 41st week. The mean values and the range of readings in late pregnancy are shown in Table IX.

The number of cases between 22 and 36 weeks is extremely small but the level of 14 to 15 g. holds for both ends of this period and the few readings available suggest that this level is probably maintained throughout.

Fig. 43 shows the red cell counts in 120 of the 145 normal cases. There is a wider variation in the counts than in the haemoglobin readings although the pattern is similar. The count rises steadily from 1.42 million at 10 weeks to 3.28 at 25 weeks. From then till 36 weeks, the results show a slow increase, but again the information available is inadequate. In the last 4 weeks the red cell counts spread out in the same way as do the

haemoglobin readings and at the 40th week counts range from 3.74 to 4.94 million, with a mean of 4.35. After the 40th week the increase continues (Table X). One count of 5.43 million was recorded with a haemoglobin of19.2 g. in a foetus delivered in the 44th week.

A study of Fig. 43 suggests that even after 23 weeks the red cell count keeps on increasing very slowly. There is an acceleration in the rate of increase from about the 37th week in association with the rapid rise in haemoglobin.

Regression lines of haemoglobin and red cells on weeks of gestation have been calculated from the normal cases and are superimposed on all scatter diagrams to demonstrate mean normal values.

(2) In Clinically Abnormal Pregnancy.

(a) In Pre-eclampsia. Fig. 44 shows the haemoglobin readings in a group of 53 foetuses, where the pregnancy was complicated by pre-eclampsia. It will be seen that most of the haemoglobin values are much higher than the normal readings for the same stage of pregnancy. In one case of severe pre-eclampsia delivered at the 29th week, the haemoglobin reading was 18.4 g. in contrast to the normal for this stage of pregnancy of 14 to 15 g. per 100 ml. On the other hand, in a mild case of pre-eclampsia delivered at 42 weeks, the haemoglobin reading was 18.6 g. which, though higher than that of the severe case delivered at 29 weeks, is still within likely "normal" limits for a foetus delivered at 42 weeks. In consideration of

the significance of the haemoglobin level in any particular foetus the stage of pregnancy must be taken into account, and the likely range of "normal" readings considered.

In 42 of the above 53 cases red cell counts were made and Fig. 45 shows that the counts are higher than normal for the stage of pregnancy reached.

(b) In Threatened Abortion and Placenta Praevia. Fourteen cases have been investigated where abortion had threatened early in the pregnancy. The haemoglobin and red cells are shown in Figs. 46 and 47. In all of these the readings are higher and some much higher than normal. The findings in 7 cases where Caesarean Section was performed for placenta praevia are also shown but in those the readings are along the normal curve.

(c) In Foetal Distress. The haemoglobin levels in 49 and the red cell counts in 31 such cases are shown in Figs. 48 and 49. In all the cases in this group the pregnancy was clinically normal; those cases with pre-eclampsia or previous threatened abortion were excluded. Many of the readings fall within the upper limits of normal, but the average is well above that of "normal" cases in whom foetal distress is absent. The large majority of readings are above 17.8 g. (120 per cent.)

The haemoglobin and red cell levels in the foetuses from the cases of toxaemia, threatened abortion and foetal distress which were delivered after the 36th week of pregnancy have been

"compared" statistically with those of the normal cases. For each group the adjusted mean levels of haemoglobin and red cells, taking menstrual age into account, were significantly higher than normal. ($P \leq 0.1$)

## (II) OXYGEN IN THE UMBILICAL VESSELS.

### (1) In Normal Pregnancy before the Onset of Labour.

The readings found in normal pregnancy are seen in Figs. 50 and 51 and Table XI.

(a) The Oxygen Capacity. The readings shown in Fig. 50 show the same pattern as the haemoglobin readings in the large series in Fig. 42. At the 22nd week the capacity has not yet reached 20 vols. At the 29 to 30th weeks it is 19.2 and 20.4 vols. respectively. At the 38th and 40th weeks it ranges between 19.8 and 22.2 vols. per cent. (haemoglobin 14.8 to 16.6 g.) and by the 42nd to 43rd weeks from 22.2 to 26.8 vols. per cent. (haemoglobin 16.6 to 20 g.)

(b) The Oxygen Content. In the period from 20 to 22 weeks the oxygen content of the blood in the umbilical vein is from 12.5 to 14 vols. per cent. In the 29th to 30th week it is still about the same level. At the 39th to 40th week the content has fallen slightly and ranges from 10.8 to 12.7 vols. By the 42nd week the content has fallen steeply, ranging from 7.8 to 9.7 vols. and the two readings at the 43rd week show a content in the vein of 6 and 8.2 vols. respectively. In readings after the 22nd week the oxygen content in the artery shows a constant correlation with that in the vein. The arterio-venous difference is between 6.2 and 7.5 vols. and as the content in the vein falls the arterial content also falls until in the 42nd or 43rd week,

the blood returning from the foetus has been deprived of nearly all its oxygen.

(c) The Percentage Saturation. At the 22nd week the blood of the umbilical vein is 75 per cent. saturated with oxygen; at the 30th week, 70 per cent., and at the 39th to 40th weeks, a little under 60 per cent. After this time the fall in saturation is very rapid and by the 43rd week the saturation may be under 30 per cent. This rapid fall is due to the combined effect of a moderate decrease in the oxygen content and a very marked rise in the capacity.

The blood in the artery is about 40 per cent. saturated at the 22nd week and about 25 per cent. at the 39th to 40th week, but by the 43rd week the saturation may fall to 3 per cent.

(2) In Normal Pregnancy after Labour.

The oxygen levels in the cord blood of the foetus after labour may be influenced by many factors, amongst which are the technical difficulty of delivery, cord entanglements, maternal anaesthesia,etc. In the results presented here the cases are as far as possible selected to avoid outside factors likely to have vitiated results. For example, spontaneous delivery was easy and the pregnancies were uncomplicated by pre-eclampsia, or bleeding, and any previous pregnancy had been normal.

(a) Spontaneous Delivery without Anaesthesia. The oxygen levels in the cord blood of a series of 10 infants are detailed in Table XII. In Fig. 52 the actual readings of the percent. saturation of the blood in the umbilical vein are plotted against the range of readings found in the normal cases before the onset of labour. This range is diagramatic and constructed from the findings in Fig. 51 and Table XI. The main points to be noted are:-

(i) The oxygen capacity, the oxygen content, and the percent. saturation with oxygen of the blood in the umbilical vein are all close to or within the range of the readings before the onset of labour, provided comparisons are made at the same week of gestation.

(ii) The arterio-venous difference in content and saturation is in the usual normal range except in two cases, where, despite an excellent venous oxygen content, practically no oxygen was found in the arteries.

(b) Prolonged or Difficult Labour. In the cases studied labour was prolonged or mechanically difficult and delivery was effected by forceps or Caesarean Section under spinal anaesthesia. The foetus had not passed meconium. The oxygen readings are detailed in Table XIII. In Fig. 53 the readings of the percent. saturation of the blood in the umbilical vein are plotted against the normal range found before the onset of labour.

(i) The oxygen capacity, and the oxygen content and percent. saturation of the blood in the vein are within the range of readings normal before the onset of labour provided comparisons are made at the same week of gestation, except in one case. In this case, labour lasted 55 hours and delivery was by difficult mid forceps; Despite the fact that the content and percent. saturation with oxygen of the blood in the vein is below the normal range, the arterio-venous difference is 6 vols. per cent., suggesting that the foetus was still obtaining adequate oxygen.

(ii) The arterio-venous difference is again within the normal range except in one case, again with a high venous and a very low arterial reading with a difference in volume of 10.6 vols. per cent. in saturation of nearly 50 per cent.

(3) In Cases where Meconium had been passed.

The oxygen levels in 11 cases where meconium staining was of recent origin or was still occurring at delivery are detailed in Table XIV. In Fig. 54 the readings of percent. saturation of the blood in the umbilical vein are plotted against the range of readings found to be normal before the onset of labour.

It is seen that:-

(a) The percent. saturation with oxygen of the blood in the umbilical vein is at or below 30 per cent. no matter the stage of gestation.

(b) This 30 per cent. is at or about the level at

which most foetuses in the 42nd and 43rd weeks begin their labours.

(c) The arterio-venous difference is on the whole very low, chiefly because there is little oxygen available in the umbilical vein. The foetuses have removed what little there is so that the blood returning to the placenta is cleared of oxygen.

(d) There is a fairly close correlation between the degree of oxygen deficit and amount of meconium passed.

(4) In Cases of Maternal Pre-eclampsia.

The oxygen levels in a series of 6 cases where pregnancy was complicated by maternal pre-eclampsia are seen in Table XV.

The severe cases were all delivered by elective Caesarean Section because of the pre-eclampsia. The moderate case was delivered spontaneously without anaesthesia.

It will be seen that:-

(a) The percent. saturation with oxygen of the blood in the vein in all cases is low for the stage of gestation because the oxygen content is low and the oxygen capacity raised. In the "moderate" case the readings, while still low, are approaching the normal range.

(b) The premature foetuses (up to the 36th week) do not appear able to remove all the oxygen from their blood. The arterio-venous difference, e.g. in one case at the 35th week of gestation, is less than 4 vols. per cent. Had the foetus

removed all the oxygen available it could have obtained 6 vols. per cent. The foetuses after 36 weeks had apparently no difficulty in clearing their blood of oxygen where necessary.

(c) Even at those low levels of oxygenation, the premature foetus in cases of pre-eclampsia, does not appear to pass meconium.

(5) In cases where there has been previous stillbirth, habitual abortion, or early neonatal death.

The oxygen levels in this group of cases are seen in Table XVI, and in Fig. 55, the percent saturation of the blood in the umbilical vein is plotted against the range found to be normal before the onset of labour. In both groups, delivery was by elective Caesarean Section before the onset of labour.

It is seen that:-

(a) Where the previous infant has been lost in the 42nd or 43rd weeks, and the present delivery is achieved before the time of previous death, the per cent. saturation with oxygen of the blood in the vein is already lower than normal for the stage of gestation. The oxygen content is, however, high and well into the normal range. The capacity is, however, higher than normal, suggesting that the content is being maintained only by a high rise in capacity.

(b) Where the previous foetus has been lost early in pregnancy, the oxygen content and saturation of the blood

of the foetus in the present pregnancy are low in all readings. The capacity is, however, higher than normal. Even though the present pregnancy has lasted longer and the foetus is born alive, there is evidence that the transfer of oxygen is still not at normal levels.

(6) The Relation between Oxygen Capacity, Oxygen Content, and Percent Saturation of the Blood in the Umbilical Vessels.

The relation between the above readings has been established by a study of 36 cases when samples were obtained before the onset of labour. This group includes normal and abnormal cases at all stages of gestation and is concerned only with demonstration of the relationship. The oxygen saturation is not an independent reading as it depends on the relation between oxygen content and capacity which were individually established.

The findings (Table XVII) show that:-

(a) The highest oxygen content is seen in association with haemoglobin levels at or about 14.8 g. per cent.

(b) Haemoglobin readings above that level are found in association with lower oxygen contents and the higher the haemoglobin the lower the oxygen content found.

(c) In view of the inverse relationship between haemoglobin (oxygen capacity) and oxygen content, there is a marked fall in the percent. saturation with oxygen of the blood in the umbilical vessels as the capacity rises so that whenever

the haemoglobin reading is over 16.5 g. (112 per cent.) the percent. saturation of the blood in the vein is likely to be well below 50 per cent. and below 20 per cent. in the artery. If the haemoglobin is over 18 g. the readings are 40 per cent. and 15 per cent. in the vein and artery respectively.

(7) The Range of Readings in the late weeks of clinically normal pregnancy.

It has been seen in Fig. 42 and Table IX that in the late weeks of pregnancy there is a fan-out of oxygen capacity readings. While the mean level shows a steady rise, there are still many cases up to the 41st week where the haemoglobin reading remains low. Correspondingly there are many where the haemoglobin reading is well above the mean level and in quite a few cases at 40 weeks, the haemoglobin is over 18 g. per cent. This would suggest that even at 40 weeks, in some cases, low oxygen levels might be found. The oxygen levels in such a case are seen in Table XVIII. It will be noted that the readings are typical of the picture more common at the 43rd week.

A study of the haemoglobin readings in Fig. 42 and the relationships between oxygen capacity and oxygen content and saturation in Table XVII have allowed construction of Fig. 56, which demonstrates the range of oxygen levels (percent. saturation) likely to be found in the blood of the umbilical vein of the live foetus in late pregnancy. Readings are more likely to be

found in the upper half of the range, and of course the higher the percent. saturation the more normal the pregnancy physiologically. It will be seen, however, that the highest readings in the 42nd and 43rd weeks are likely to be 45 per cent. and 35 per cent. respectively. The readings quoted in Fig. 51 and Table XI are all in the upper range of the likely readings and demonstrate the normal physiological pattern.

(8) Other Factors influencing oxygen levels.

It may be difficult to say whether a low content of oxygen is due to a sudden accident during delivery or to a pathological process which has existed for some time before delivery was performed. When, at Caesarean Section before the onset of labour, an unexpectedly low oxygen content is found (when the content is related to the oxygen capacity), a recent and temporary interference with the oxygen supply should be suspected. In Tables XIX and XX examples are shown.

(a) Drop in Maternal Blood Pressure. If under the influence of spinal anaesthesia the maternal systolic pressure should fall below 80 to 90 mm. of mercury and should remain low for some minutes before the child is delivered, the transfer of oxygen to the foetus is impaired and may cease because the effective placental pressure (see page 16) becomes negative. In practice any risk of a blood pressure drop is minimised by the preliminary injection of "Methidrine", or the drop is controlled

by methidrine. It will be seen, however, from the results of Table XIX that the percent. saturation with oxygen of the blood in the foetal vessels may easily drop 10 to 20 per cent. (see page 22).

(b) Difficulty in Extraction of the Child. When during the course of Caesarean Section, there is delay and difficulty in extracting the foetus through the uterine incision, or the umbilical cord is pulled or compressed during the delivery, the oxygen levels are often 10 to 20 per cent. lower than expected. (See Table XX).

## (III) ADULT TYPE OF HAEMOGLOBIN IN THE BLOOD OF THE FOETUS.

The proportion of adult type of haemoglobin in the blood of the human foetus throughout gestation is seen in Fig. 57. In normal pregnancy the adult type first appears at about the 13th week, when it constitutes about 1 to 2 per cent. of the total haemoglobin. The proportion rises to reach 10 per cent. at or about the 20th week and appears, from the few cases available, to remain close to that level till the later weeks.

At 35 weeks, the readings begin to spread out, and by 40 weeks the range is 11 to 39 per cent. with a mean of 22.2 per cent. When pregnancy lasts beyond the 40th week, the proportion of adult haemoglobin rises, till at 42 weeks the mean reading is 30.7 per cent.

In the clinically abnormal pregnancy (pre-eclampsia, previous threatened abortion, foetal distress), it is seen that the proportion of adult haemoglobin is unchanged from the normal, and corresponds to the expected level for the stage of gestation reached. I have shown that in such abnormal pregnancies the haemoglobin reading is much above normal levels (page 87 ). It would appear, therefore, that when anoxia forces the production of extra red cells, the haemopoetic tissues produce an increased number of each of the various types of cell in the same proportions as they were producing before extra haemopoesis occurred. The proportion of cells containing adult haemoglobin is unchanged,

even though the amount of haemoglobin in each unit of blood may rise by 30 per cent.

Dr. Turnbull, who pursued this investigation further at my request, found no correlation between the proportion of adult haemoglobin and haemoglobin level, red cell count, or foetal weight. It appears that the amount of adult haemoglobin is a function purely of the age of the foetus. The postmature foetus has more adult haemoglobin than the foetus at term because it is older, and not because of its deteriorating oxygen environment.

There is a correlation, however, between the percentage of adult haemoglobin and the number of red blood cells 7.5 mu and under in size. It is possible that those are the cells which contain adult haemoglobin.

## (IV) OBSTETRIC DEATH.

### (1) The Effect of Parity and Maternal Age.

The effect of parity on the obstetric death rate is seen in Table XXI. The death rate is highest in a first pregnancy, much less in the second, and rises steadily thereafter. The high rate in first pregnancies is due to an excess of deaths from difficult labour (with the vertex presenting) and from toxaemia and deformity, and to a much lesser extent from "mature, unexplained." The incidence of all obstetric death groups has been shown in this table to illustrate the classification in use and to show the relative importance of each cause group.

The effect of parity and maternal age on the cause groups relevant to the subject of the thesis will now be discussed.

(a) Mature Unexplained. The rate is highest in first pregnancies and in later pregnancies is a little lower and is unaltered by high parity. (Table XXI). In Table XXII and in Fig. 58, it is seen that in primigravidae the rate rises steadily from 2.5 per 1000 in the age group 15-19, to 20.4 in the age group over 35. The adverse effect of age is less marked in multigravidae. (Table XXIII).

(b) Difficult Labour (with the vertex presenting). The death rate directly due to difficult labour (trauma (vertex) and StrA) is high in a first pregnancy and very low thereafter (Table XXI). In Table XXII and Fig. 58 it is seen that in primigravidae the death rate rises steadily from the age group 15-19 till the age group 30-34. The fall in the age group 35 and over reflects the increasing use of Caesarean Section in the older primigravida in an effort to ensure a live child. In multigravidae the rate rises sharply after the age of 35. (Fig. 58 and Table XXIII).

(c) Toxaemia. In Table XXI it is seen that the death rate is lowest in the second, third and fourth pregnancies and about equally high in first and in seventh and subsequent pregnancies.

Table XXII shows that in primigravidae the rate is lowest in the age group 20-24, and rises quickly with age, particularly after 29.

In a separate study of Aberdeen Maternity Hospital primigravidae (Nelson, 1954), it has been shown that although the incidence of mild pre-eclampsia rises steadily from 14.7 per cent. in age group 15-19 to 30.8 per cent. in the age group over 35, moderate or severe pre-eclampsia rose only from 3.9 per cent. in the age group 15-19 to 5.0 per cent. in the age group 35 and over. Fig. 59, compiled by Nelson, shows that the incidence of obstetric death in cases of mild pre-eclampsia is identical with the general

obstetric death rate and behaves similarly with rising maternal age. The obstetric death rate in cases of moderate or severe pre-eclampsia, however, behaves very differently. It is high in young women under 20, low in the age group 20-25, and rises very steeply thereafter so that over the age of 35 a primigravida with moderate or severe pre-eclampsia has a 30 per cent. chance of losing her child. The death rate of the foetus in pre-eclamptic pregnancies is therefore mainly associated with the severe forms of the disease. Since the incidence of severe pre-eclampsia is little altered by maternal age, we cannot explain the high rate in primigravidae under 20. The rising rate with rising maternal age is due primarily to the age of the mother and not to any greater incidence of the severer forms of the disease.

In multigravidae (Table XXIII) it is seen that, while there is a rise in the rate with age, the rate under 20 is again very high. (The numbers are, of course, very small).

(2) The Influence of Length of Gestation.

(a) All Obstetric Deaths. The obstetric death rate by length of gestation is seen in Fig. 60 and Tables XXIV and XXV, which are constructed from a study of the deaths occurring in 4364 primigravidae and 6687 multigravidae booked for and delivered in the Aberdeen Maternity Hospital from 1948 to 1952. It is seen that the obstetric death rate is very high for deliveries up to the 38th week of pregnancy and is lowest in primigravidae for delivery in the 41st week, at which time it is 11.7 per 1000 total births. The rate rises thereafter to

reach 38.6 per 1000 for deliveries at or after the 43rd week. The rise after term is due mainly to an increase in stillbirths, but the first week neonatal death rate, which is 3.9 for deliveries in the 41st week, rises thereafter to reach 9.6 for deliveries in the 43rd and subsequent weeks.

In multigravidae, the rate is 9.4 per 1000 total births for deliveries in the 40th week, but two and a half times greater for deliveries in the 43rd and subsequent weeks. The rise here is due almost entirely to a rise in stillbirths, but the neonatal death rate rises from 3.6 at 40 weeks to 5.6 at 43 weeks.

(b) The Types of Obstetric Death. The rise in the obstetric death rate after the 40/41st weeks is seen in Fig. 61 and Tables XXIV and XXV, to be due primarily to a rising incidence of unexplained deaths (M.U.) Deaths of this type are uncommon at the 40/41st weeks, but are, by 43 weeks, in all parities the highest single cause of death. In primigravidae there is also a rise in incidence of deaths considered to be directly due to difficult labour with the vertex presenting (i.e. trauma (vertex) and anoxia under stress). The death rate from other causes is also raised in the 42nd and 43rd weeks.

In the above series of booked hospital cases in 1948 to 1952, death rates by each week of gestation could be calculated, as special care was taken to establish accurately the duration of pregnancy. Exclusion of deaths in cases where the gestation period was uncertain does not influence the picture at or after

term as most of them are in premature foetuses. Although the facts are accurate, the actual number of deaths is so small that when they are broken down into cause groups, numbers are too small for statistical analysis with significance. In view of this, all stillbirths and first week deaths occurring in a much bigger series, (10758 primigravidae and 12723 multigravidae, booked for and delivered in Aberdeen Maternity Hospital from 1938 to 1951) have been studied. The proportion of deaths from each cause in relation to the total deaths occurring at each week of gestation has been calculated. Death rates could not be calcul-:ated as accurate information is not available of the gestational age of all deliveries, but in the cases in which obstetric death occurred, special care was taken to determine that the length of gestation was accurate.

Table XXVI shows that the proportion of "Mature unexplained" deaths rises steadily as pregnancy is prolonged until, by the 42nd and subsequent weeks, at least one third (32.4 per cent.) of all deaths are "unexplained" in contrast to 16.7 per cent. at the 40th week.

The proportion of total deaths due to "Mature unexplained" group is about equal in primigravidae (14.4 per cent.) and multigravidae (12.8 per cent.)

Table XXVI shows the proportion of deaths considered to be directly due to difficult labour (trauma (vertex) plus anoxia under stress). It will be noted that the proportion of deaths

(14.0 per cent.) from this cause in primigravidae is much higher than the proportion in multigravidae (4.3 per cent.) The proportion due to difficult labour of all deaths occurring in each week of gestation is fairly steady up to the end of the 41st week, but after that time in primigravidae 37.1 per cent. of all deaths are due to this cause.

If the group due to difficult labour in primigravidae is subdivided into the trauma (vertex) group, when death is due to cerebral birth injury, and the "anoxia under stress" group, when death is anoxic, it is seen (Table XXVI), that the rising proportion after the 40th week is due almost entirely to a great increase in deaths from anoxia. It is also seen that deaths from anoxia in prolonged labour (anoxia under stress) are extremely uncommon before the end of the 40th week of gestation, and that 83 per cent. (25 out of 30) of them occur after the end of the 41st week.

(3) Causes of Obstetric Death after the 41st week.

Table XXVII shows the causes of obstetric death after the 41st week of gestation for the cases in the 1938 to 1951 series of primigravidae.

As has already been noted, the most important single cause is the "Mature unexplained" group, next anoxia associated with prolonged labour "anoxia under stress", and after that all forms of trauma (difficult vertex; malpresentation; cord, etc.) Pre-eclampsia has become unimportant by this stage of pregnancy,

and deformity is a less frequent cause than at earlier stages of gestation.

Summary.

(1) Obstetric death of mature babies from causes clinically unexplained, but with autopsy signs of anoxia, is slightly more common in first pregnancies. Such deaths are much more likely in older primigravidae. Uncommon before the 40th week of pregnancy, they are seen increasingly more often as pregnancy becomes prolonged, and by the 43rd week are the most common type of obstetric death. They are responsible for 14.4 per cent. of all obstetric deaths in primigravidae, and 12.8 per cent. in multigravidae.

(2) Obstetric death from anoxia, during or after prolonged labour, is much more common in first labours because of the greater frequency of prolonged labour. Such deaths are much more likely in older primigravidae. Very uncommon before the 40th week of pregnancy, they are seen increasingly more often as pregnancy becomes prolonged, and by the 43rd week are, in primigravidae, responsible for nearly one-quarter of all deaths. They are responsible for 6.5 per cent. of all obstetric deaths in primigravidae and only 1.7 per cent. in multigravidae.

(3) Obstetric death from birth trauma during or after difficult labour is more common in first labours. Such deaths are much more likely in older primigravidae. They are seen at any time after the 38th week of pregnancy, but as pregnancy in primigravidae becomes prolonged they occur more frequently. The proportion of deaths due to this cause by the 42nd week is 13.3 per cent., the same as at 40 weeks, but there are likely to be at least three times more deaths in the 42nd week. They are responsible for 7.5 per cent. of all obstetric deaths in primigravidae, and 2.6 per cent. in multigravidae.

(4) Obstetric death from toxaemia is directly related to the severity of the disease as judged by the degree of albuminuria. Somewhat more common in primigravidae, such deaths are much more common the older the mother after the age of 20 (under 20 there is a high death rate). They are very uncommon after the 40th week of pregnancy, and they are responsible for about 10 per cent. of all obstetric deaths.

## (V) FOETAL DISTRESS.

### (1) The Incidence of Foetal Distress by Week of Delivery.

(a) By Type of Labour. The incidence of foetal distress in all labours in primigravidae is seen in Fig. 62 and Table XXVIII. It is low up to the 40th week, being only 8 per cent. The rate thereafter rises steadily till, at the 44th week, evidence of distress is shown in 25 per cent. of labours. In "normal" labours (see page 115 ), the rate is only a little lower, the rise begins in the 41st week, and by the 44th week is 21 per cent. The "distress" incidence in cases of difficult labours (with the vertex presenting) (see page115) is, however, high. At 40 weeks, 13 per cent. of foetuses undergoing difficult vertex labour show clinical evidence of distress, and there is a steady rise in incidence to nearly 40 per cent. in the 43rd week.

The incidence of all labours in multigravidae is seen in Fig. 63 and Table XXX. There is a steady rise from the 38/39th week when the incidence is 5.6 per cent. of all labours, to 12.1 per cent. in the 43rd and subsequent weeks.

(b) By Type of Distress. Both in primigravidae and in multigravidae it is seen, (Figs. 63 and 64, and Tables XXIX and XXX) that the rising incidence in the later weeks is due mainly to an increase in the incidence of meconium staining of the liquor amnii.

In primigravidae only, there is, after the 40th week, an increase in the incidence of cases in which slowing or irregularity of the foetal heart is the only sign of distress. The increase is not progressive with increasing length of gestation as clearly as is the rising incidence of meconium.

(c) By Clinical Cause of Distress. In primigravidae it is seen (Fig. 65 and Table XXIX) that the incidence of distress from all causes is low up to the 39th or 40th week and rises thereafter.

When distress is due to prolonged labour or to pressure on the foetal head in the pelvis (combined in Fig. 65), the rising incidence after term is due to a great extent to the rising incidence of difficult labour which occurs after that time (see page 115). The incidence of distress due to cord complication also rises to some extent. Distress occurring in the second stage with the foetal head on the perineum is also a little more frequent after term.

The most marked and constant rise, however, is in those cases of distress for which no clinical cause can be found, and after the 41st week this is the greatest single cause of distress.

If the foetus, after the 41st week, is very likely to show distress without obvious clinical cause, then a certain amount of the rise in the distress rates due to "cord" and "difficult labour" is probably associated with falling ability of the foetus to stand any stress whatsoever.

In multigravidae (Fig. 66 and Table XXX), it is seen that the incidence of distress from most causes is very low mainly because of the very low incidence of difficult labour. The incidence of distress for which no clinical cause can be found rises sharply after 38/39th week and is the main cause of the rising incidence of distress in prolonged pregnancy. Table XXXI and Fig. 67 show that, in primigravidae and multigravidae, the incidence of clinically unexplained distress is very alike at each week of gestation. This suggests that the "cause" of the clinically unexplained group must operate alike and equally in all parities.

(2) The Relation between Clinical Cause and Type of Distress (Table XXXII).

In primigravidae the passage of meconium is the sign of foetal distress in 95 per cent. of the clinically unexplained group, and in more than 70 per cent. of cases where distress was due to prolonged labour. About half the cases of distress due to interference with the umbilical cord will show meconium and much less than half of the cases in which pressure on the foetal head in the bony pelvis was considered the cause of the distress. Second stage distress by definition should include few if any cases of meconium staining.

In multigravidae, because of the greatly decreased incidence of mechanical pressure on the foetus, meconium is a relatively more common sign of distress.

(3) The Effect of Maternal Age on the Incidence of Foetal Distress.

In Fig. 68 and Table XXXIII, it is seen that the incidence of distress rises with the age of the mother in primigravidae. The incidence in difficult labour, however, shows a slight fall up till the age of 29, and a rapid rise thereafter.

In Fig. 69 and Table XXXIV, it is seen that the trend with age is less uniform in multigravidae, especially after the second pregnancy.

In Figs. 64 and 69 and TableXXXV, it is seen that the incidence of both types of distress rises with advancing maternal age, and that an increase in meconium staining is mainly respons-:ible for the high rate in the older age groups.

(4) The Relation between Maternal Age and Week of Delivery.

The rise in incidence of foetal distress with rising maternal age and the rise with prolongation of pregnancy are independent of each other. In Fig. 70 and Table XXXVI is seen the incidence by week of delivery of foetal distress in various age groups. It is seen that after the age of 20 there is a steadily rising incidence as pregnancy becomes prolonged. The rapidity of the rise and the total incidence after the 40th week is greater the older the mother, and is very marked in primigrav-:idae over 35.

Summary.

(1) The foetus is much more likely to show "distress" in primigravidae and in difficult labours.

(2) In all parities the incidence of distress increases with rising maternal age and, in all parities, all age groups, and in all labours the incidence rises the longer pregnancy is prolonged after the 40th week.

(3) The rising incidence after the 40th week and with rising maternal age is due mostly to the increasingly frequent appearance of meconium.

(4) Distress without obvious clinical cause, and distress during prolonged labour, is mostly manifest by the passage of meconium. (often without any irregularity or slowing of the foetal heart).

(5) Distress due to undue pressure on the foetal head in the bony pelvis or, if the head is held up on the perineum, is usually manifest by slowing or irregularity of the foetal heart without meconium staining.

(6) In multigravidae, unexplained meconium staining is seen just as frequently as in primigravidae. Foetal heart signs are uncommon in multigravidae because undue pressure on the foetal head is unusual and it is rarely held up by the perineum.

(7) The foetus, in primigravidae, will pass meconium in at least 17 per cent. of labours at the 44th week, and in 20 per cent. of all labours where the mother is over 35 years of age.

## (VI) DIFFICULT LABOUR.

Since 1948, in the Midwifery Department of the University of Aberdeen, labour has been classified for research purposes into three groups - normal labour, minor difficult and major difficult labour. All labours ending spontaneously in less than 24 hours are normal and all others are "difficult." The degree of difficulty depends on the effect of the labour on the mother, the duration of labour, and the type of delivery. (Cases of malpresentation and multiple pregnancy are treated separately, Caesarean Section or forceps delivery performed because of foetal distress, maternal eclampsia, placenta praevia, etc., are excluded from the labour assessment.)

In Fig. 71 it is seen that the incidence of difficult labour in primigravidae rises steadily from the 37th to the 44th weeks. The rise is due entirely to an increasing incidence of a major degree of difficulty. At the 40th week only 3.1 per cent. of all cases have a major degree of difficulty in labour or delivery, but by the 44th week the figure rises to 13.7 per cent. This rise is due mainly to an increase in uterine dysfunction of severe degree but mechanical difficulty also rises probably because it is made more serious because of the less efficient contractions.

It will be seen that, after the 40th week, the foetus already with a failing oxygen supply is much more likely to be

called upon to undergo a major degree of difficulty in labour. A rising incidence of difficult labour after term has been noted by Rathburn (1943), de Lee and Greenhill (1947), Beruti and Roust (1948), Reenkola (1948), Stewart (1952) and Clayton (1953).

## DISCUSSION.

(I) Findings.

(II) Application of the Results to the Clinical Practice of Obstetrics.

(III) Significance of the Results in a Study of the Physiology of the Foetus.

(IV) Advancing Maternal Age.

(V) Importance of the Findings in a Study of the Long Term Effects of Anoxia.

(VI) Oxygen Supply in Early Pregnancy.

---

## (I) FINDINGS.

### (1) The Accuracy of the Experimental Findings.

The accuracy of the findings is discussed from two view points -

Are the findings experimentally correct? Do the readings represent the actual haemoglobin or oxygen levels in the blood of the cord segment?

When samples were obtained at Caesarean Section, do the findings represent the condition in utero immediately before operation?

(a) Haemoglobin. King et al (1948a) found the commercial instrument accurate to 5 per cent. when tested against base line readings. The individual apparatus used by me was found to be uniformly accurate over the whole scale from 50 to 150 per cent. The readings were duplicated and often from blood samples from different vessels in the same foetus and agreed to 2 per cent. Even if errors were additive (which is extremely unlikely over a large series of cases) any given reading could not be more than 5 to 7 per cent. out from the true content. The variation in readings which I have considered to be of significance is at least 10 per cent. and at the most

about 40 per cent. Error from method technique or sampling would not vitiate the findings.

(b) Oxygen. The method is accurate to 0.25 vols. per cent. and the readings to 0.5 vols. per cent. The error in any given sample is therefore much less than 1 vol. per cent. Since the differences I have claimed to be significant are from 4 to 10 vols. per cent., experimental error would not have been responsible for the difference in the findings.

Individual readings are likely to be accurate, as oxygen and haemoglobin findings can be duplicated under a given set of clinical circumstances. Clinical groups will provide closely similar readings within the group pattern and different from the patterns of other groups, and as is discussed later, there is an inter-relationship between oxygen readings and haemoglobin, which is maintained throughout the series.

(i) Samples at Caesarean Section. The oxygen levels claimed to represent conditions before the onset of labour have been obtained from the blood in a segment of umbilical cord isolated between clamps immediately on delivery of the child. It is possible that, in the short period between incision of the uterus and obtaining the sample, there is some loss of oxygen since the placental site must contract when the uterus empties.

Barcroft (1946) considers that in work of this type the highest levels of oxygen content found are more nearly correct as interference with the uterus or cord circulation will lower the oxygen readings. Eastman (1930) and Dieckman and Kramer (1944) sampled the blood in the umbilical vein through a small uterine incision with the foetus still in utero. Top readings of 13.3 vols. per cent. and 12.8 vols. per cent. respectively were found. Haselhorst and Stromberger (1930), with a technique similar to that used by me, found a top reading of 13 vols. per cent. In a series analysed at 39/40 weeks' gestation, I found a top reading of 12.7 vols. per cent. I consider, therefore, that any fall in oxygen content due to extraction of the foetus, if it exists at all, must be of the order of 0.5 vols. per cent, (the difference between Eastman's reading and my top reading).

(ii) Conditions in Utero in Late Pregnancy.

It is difficult to be certain whether the findings at Caesarean Section necessarily represent the actual levels of oxygen present in the unopened uterus under physiological conditions. Under present circumstances it is impossible to answer this question.

Readings obtained by Barcroft and his colleagues (1939) were obtained under similar conditions and a spinal anaesthetic was used for the ewe. They considered that the levels and pattern

found were truly representative, consequently the findings presented here are just as likely to be representative of conditions pertaining in the unopened uterus in the pregnant woman.

(2) Haemoglobin and Red Cells.

I have shown that, in the human foetus, the red cell count increases steadily throughout pregnancy. In the majority of infants at birth, the normal adult level is not yet reached. The haemoglobin reaches normal adult levels by the 22nd to 24th week, and may remain there till delivery at term. In many cases after the 37th week, however, the haemoglobin level again increases and there is an acceleration in the rate of increase of red cells, and both may be very high, especially if pregnancy continues to the 43rd week.

There appear to be two main factors responsible for the development of the blood picture seen in the human foetus at birth. The first is concerned with the normal growth and maturation of red cells, and the development of the oxygen carrying power of the blood.

(a) Growth and Maturation. The normal adult level of haemoglobin is reached by the 22nd to 24th week and remains at that level (14.8 to 15 g. per 100 ml.) till delivery at term.

The red cell count at the 22nd to 24th week is 3.0 million per c.cm., at 36 weeks is 3.5 to 3.7 million per c.cm., and at

term is 3.74 to 4 million per c.cm, provided the haemoglobin level is still 14.8 to 15 g. per/100 ml. The red cell count keeps rising steadily. Work by Dr. Elizabeth Turnbull (unpublished) shows that, in the human, as in most mammals (Wintrobe and Shumacker, 1935, 1936) the mean cell volume and mean cell diameter is decreasing as pregnancy progresses, fewer large cells and more small cells entering the circulation. At term, however, the mean size is still above normal adult levels. This is the normal growth and maturation picture. I have shown that the highest oxygen content and percent. saturation is found at term in association with haemoglobin levels at or about 14.8 to 15 g. per/100 ml. The growth and maturation picture in the human is the same as for other mammals except that the haemoglobin reaches adult level at a relatively earlier stage of pregnancy.

(b) Response to Anoxia. In the late weeks of pregnancy, however, in most mammals and in the human foetus (Figs. 42 and 43; Tables IX and X), the haemoglobin levels tend to rise above normal adult levels. The rise in mean levels becomes greater as pregnancy is prolonged after term, but there is no uniformity and higher levels may be found at 40 weeks in some cases than at 43 weeks in others. The highest levels are, however, found in the 42nd and 43rd weeks. This

rise in haemoglobin is produced by a great acceleration in the production of red cells. There may be more than 5.0 million per c.cm. in some cases. After the 36th week, therefore, some new factor appears to be added to the normal growth picture, and this new factor stimulates an increase in the number of red cells. The size of the increase varies very much from foetus to foetus but tends to be greater as pregnancy continues. The red cell count may be increased at 40 weeks from the normal level of 4 to 4.9 million per c.cm. while the haemoglobin increases from a normal 15 to 18.6 g. per 100 ml. - both about a 25 per cent. increase over the normal growth level.

This increase in cells could be achieved by a loss in fluid from the blood or by an increase in circulating cells. Without adequate blood volume studies in the foetus, we cannot say whether a shift in the disposition of body fluids does occur but a change of this magnitude seems unlikely.

Before the onset of labour, high haemoglobin readings are found only in association with a lower than normal percent. saturation and usually a lower than normal oxygen content in the umbilical vessels. This is a strong argument against the theory that increase of red cells and haemoglobin in the blood is due to haemoconcentration. It is also unlikely that a continued and uniform increase in the number of red cells in association with a falling oxygen supply could be achieved by

the mobilisation of red cells from reservoirs such as the spleen, firstly because of the size of the increase, and secondly because of its constant and uniform nature.

Barcroft et al (1939) and Barcroft (1946) attributed the rise in the haemoglobin of the sheep foetus in the latter weeks of pregnancy to increased production of red cells from the marrow in response to a falling oxygen supply, and found a close correlation between the haemoglobin level and the percentage saturation of the blood in the umbilical vessels.

In Table XVII it is seen that in the human foetus a close correlation also exists between haemoglobin level and oxygen content and saturation in the umbilical vessels. It is likely that the increase in red cells and in haemoglobin is a response by the foetus to a falling oxygen supply. Individual variations in haemoglobin and red cell count can be explained by individual variations in supply. The increase in mean readings with prolongation of pregnancy is explained by a constantly falling oxygen content and saturation (Figs. 50 and 51).

(c) Comparison with other workers. The findings in clinically normal cases compare with those quoted in Table V and discussed in page 32. In my series, for all foetuses delivered from the 37th to 43rd weeks the mean haemoglobin value is 17 g. per 100 ml. and mean red cell count 4.41 million with ranges of 14.8 to 20.5 g. and 3.52 to 5.24 million per c.cm.

The haemoglobin and red cell values at birth depend on the duration of pregnancy and the degree of intra uterine anoxia to which the foetus has been subjected. This finding adequately explains the scatter of readings obtained by myself and other workers.

(3) The Oxygen Supply in the Umbilical Vessels in Normal Pregnancy before the Onset of Labour.

(a) Significance of the Findings. The findings in Table XI and Figs. 50 and 51 show that at 40 weeks the well oxygenated foetus has in the blood of the umbilical vein nearly 100 per cent reserve of oxygen content, available to meet sudden emergency. The foetus removes 6 or 7 vols. from each 100 ml. of blood. returning 5 or 6 to the placenta. So long as 6 to 7 vols. are available in the blood, the normal foetus can obtain that amount because of its ability to clear the blood of its contained oxygen. At 43 weeks, for example, no oxygen is returned to the placenta. Despite the ability of the foetus to extract 6 to 7 vols. when the content in the vein is at that level, a certain degree of tissue anoxia must exist as soon as the content falls much below 12.5 vols. per cent, since the haemoglobin level begins to rise. At 40 weeks, when the content is over 12 vols. and the haemoglobin is still at 14.8 g. the saturation is at or above 60 per cent. At those levels, tissue oxygenation is adequate. At any stage of pregnancy a content or saturation below those levels is

accompanied by a rise in haemoglobin due presumably to a fall in the tension of oxygen in the blood reaching the haemopoetic tissues.

As with the acclimatised adult, increase in oxygen capacity may return the content to normal, and contents over 12 vols. per cent are seen in association with haemoglobin readings of 16.4 g. and 18.2 g. (Tables XI and XVI). If the oxygen supply available at the placenta continues to decrease, the content is not maintained, despite a continual rise in capacity, and the percent saturation falls rapidly (Fig. 50). If the saturation falls below 30 percent the foetus will pass meconium even though, in some cases, it is still able to extract 6 to 7 vols. from each 100 ml. of blood and is actually returning oxygen to the placenta (see Table XIV). Such a pattern is very similar to the oxygen state of the adult with polycythaemia secondary to cardiac shunts. Such a person is severely handicapped because his blood has a very low saturation with oxygen, even though oxygen content is within normal limits.

(b) Comparison with Findings of Other Workers.

The findings of Eastman (1930), Haselhorst and Stromberger (1930, 1931) and Dieckman and Kramer (1944) (see pages 7 to 10), resemble closely the oxygen findings presented here. The highest levels of oxygen content and saturation found by them are the same as those shown here to be characteristic of the highest levels at any time from the 30th to 41st weeks of pregnancy.

Previous authors have not, however, noted the durations of pregnancy nor have they necessarily selected clinically normal cases. In only a few instances is the oxygen capacity or percent. saturation quoted, so that no correlation between the two can be studied.

The findings presented here confirm that in the human foetus there is, as in the goat (Barcroft et al, 1934), sheep (Barcroft et al, 1939b) and rabbit (Barcroft and Young, 1945; Snyder, 1949) (see pages 2 to 5) a fall in the oxygen content of the blood in the umbilical vessels in late pregnancy which is accompanied by a rise in the level of haemoglobin. If pregnancy proceeds beyond normal term, the fall in oxygen supply becomes more marked, the haemoglobin rises to very high levels and the percent. saturation of the blood with oxygen becomes very low.

(c) Comparison with Altitude Response in Adult.

Barcroft (1938) considers that the adult acclimatises to altitude by (1) increased pressure of oxygen in alveolar air by hyperventilation, (2) increase in haemoglobin, and (3) acceleration of blood flow. The total effect minimises the bad effects of a lowered partial pressure of oxygen and returns both the oxygen content of the blood and the mean capillary oxygen tension to normal, even though the percent. saturation of the arterial blood may remain at below 85 per cent.

In the foetus, (1) is not possible, (2) does occur, (3) there is no evidence that the foetal heart rate rises in

late pregnancy, in fact all the evidence is to the contrary.

As already discussed, however, the main problem for the foetus is that the supply at source continues to deteriorate and it is in the position of an adult who climbs steadily to higher and higher altitudes without a rest period in which to acclimatise.

(4) Oxygen in the Umbilical Vessels in Abnormal Pregnancy.

In the abnormal conditions studied the haemoglobin levels and red cell counts have been higher and the oxygen levels lower than normal for the stage of gestation, suggesting that one effect at least of the clinical abnormality has been to interfere with the transfer of oxygen to the foetus.

(a) Pre-eclampsia. There is interference with the oxygen supply to the foetus and the degree of interference parallels the severity of the disease as judged by the degree of albuminuria. In mild cases, the interference is slight. In "severe" cases a great reduction in oxygen levels appears to stimulate the foetus even at about 31 to 32 weeks to a 50 per cent. increase in haemoglobin and red cells. In cases of "fulminating" eclampsia examined at the 23rd to 25th weeks, the haemoglobin and red cells were at normal levels, suggesting that the foetal response takes some little time to develop.

It has been shown that placental degenerative and age changes take place earlier and to a greater degree in pre-eclampsia and parallel the degree of albuminuria (pages 28 to 29), that the rate of transfer of diffusible nutrients is much depressed in

pre-eclampsia (pages 30 and 31) and by Brown and Veall(1953) that the rate of placental blood flow is slowed. Transfer of oxygen is now shown also to be depressed. It is not possible, however, to say whether the fall in transfer of oxygen and other nutrients is due solely to the placental changes or whether both are secondary to slowing blood flow associated with alteration in decidual and other vessels as described by Zeek and Assali (1950) (page 29). The premature infants (up to the 36th week) (Table XV) failed to extract adequate oxygen from their blood even though in some cases sufficient was apparently available. There is no obvious explanation and this phenomenon requires confirmation and much further study.

(b) Threatened Abortion earlier in the Pregnancy and Placenta Praevia. The haemoglobin and red cell findings in Figs. 46 and 47 suggest that when abortion threatens earlier in the pregnancy, firstly, that premature delivery is fairly common, and secondly, that there is continued interference with the oxygen supply to the foetus as at delivery the haemoglobin and red cell levels are much higher than normal. It is signif-:icant that where the reason for the bleeding is shown later to be a placenta praevia, the haemoglobin and red cell readings are at normal levels, possibly because the bleeding in placenta praevia was due to a mechanical separation of a small piece of

placenta and unlikely to affect placental function as a whole.

It is not possible at present to explain the mechanism of persistent interference with foetal oxygen supply following threatened abortion. Possibly the vascular defect primarily responsible for the initial bleeding is only part of a general vascular defect which prevents adequate nutrition in late pregnancy and predisposes to premature onset of labour.

(c) Obstetric Death in the immediately previous pregnancy. The findings in Table XVI and depicted in Fig. 55 are in some ways not unexpected in the light of clinical experience. Repeated intra uterine death or premature delivery of an infant which dies neonatally is not too uncommon. In many cases progressive improvement occurs and eventually a live child is born at term.

The findings, however, show that even if the pregnancy is successful, a defect in transfer of oxygen still exists.

The mechanism of failure of the pregnancy and of the improvement with practice is obscure. The answer may lie in stimulation of uterine vascular development by each pregnancy till a sufficient response is obtained to carry an infant successfully, but why the initial response is insufficient, and how stimulation occurs is unknown.

In each of the cases quoted in the second half of Table XVI the previous infant had been lost from a postmature anoxic syndrome, either in utero or immediately after birth. In the

current pregnancy the oxygen capacity is far above normal levels for that stage of pregnancy. If one assumes a degree of improvement in the pregnancy studied, the oxygen supply in the first pregnancy must have been very much worse even at the stage of pregnancy now studied and death of the foetus from anoxia easily explained.

Two of the cases show clearly the mechanism of acclimatis-:ation (2959/50 and 2195/52). At the 39th week of gestation the oxygen supply has been falling faster than in normal cases, increase in oxygen capacity has been forced but this is still able to maintain the oxygen content in the vein at normal levels 13.8 and 11.1 vols. per cent. The saturation, however, falls in view of the rising capacity. Had the pregnancy been allowed to progress further, the persistent fall in oxygen available would have stimulated even further haemopoesis, but it is doubt-:ful if the content could have been maintained. The saturation would have continued to fall.

In Case 513/51, elective operative delivery was probably performed just in time, as a further week would probably have seen sufficient deterioration in the foetal oxygen supply to have promoted death of the foetus.

(5) The Oxygen in the Umbilical Vessels after Labour.

(a) After Spontaneous Delivery without Anaesthesia.

The findings of previous authors are summarised in Table II and my findings in Table XII and Fig. 52. If mean levels of oxygen findings are considered, it is seen that the readings of the current investigation agree very closely with all those of previous investigators with the exception of the findings of Goldbloom and Gottleib (1930), who found much higher readings. It is not possible to explain why the readings of those authors were so high. A study of their article shows that in the nine cases, the total scatter in saturation was only 6 per cent. (76 to 82). The results seem too uniform to be correct.

The real importance of results found after spontaneous delivery is (1) as an indication of the oxygen levels at which most infants begin life, and (2) as an indication of the effect of normal labour on the oxygen supply to the foetus.

(1) It seems probable that the infant born after normal spontaneous delivery at term begins life with its blood about 50 per cent. saturated with oxygen. In Case 412/51, little or no oxygen was present in the umbilical artery. In this case, the head had been arrested by impaction of the shoulders and the head was almost black in colour before delivery. Extreme foetal heart slowing allowed extraction of most of the oxygen. The foetal levels of oxygen at birth are a base line in studies of the factors influencing the onset of normal respiration, but will not be further discussed here.

(2) Previous authors (pages 8 and 9) have shown that normal labour has little effect on the oxygen supply to the foetus and the results shown here confirm that finding. Unless the period of gestation is considered and normal cases only are studied, it is easy to draw false conclusions, as levels after normal spontaneous delivery at 40 weeks in normal cases might be much higher than those found before the onset of labour in pre-eclampsia or in normal cases at the 43rd week, but this cannot be taken to mean that labour enhances the supply of oxygen to the foetus.

It is only to be expected that normal labour should have no deleterious effect on the oxygen supply, since it is a physiological process. Before the onset of labour, the foetus is already (even at 40 weeks) living in a deteriorating oxygen environment and if normal labour did depress the supply to any extent, many babies would be born dead.

(b) <u>After Prolonged or Difficult Labour</u>. The series of readings in Table XII and Fig. 53 show that even prolonged or mechanically difficult labour with instrumental delivery may not interfere with the oxygen supply to the foetus. The findings show that when the foetus begins labour with a good supply of oxygen, that supply will be maintained throughout most labours and even in the presence of some degree of disproportion or malposition, and difficult forceps delivery. It would seem

reasonable to expect that the physiology of labour would ensure that adequate reserves were available so that the oxygen supply to the foetus could be maintained under most circumstances. There are, however, no studies in the literature with which the readings obtained here may be compared.

(6) Oxygen in the Umbilical Vessels when the Foetus passes meconium.

The oxygen readings in Table XIII and Fig. 54 should be studied along with the haemoglobin and red cell readings in Figs. 48 and 49, with the clinical statistics of distress in Figs. 62 to 70 and Tables XXVIII to XXXVI, and with the summary on page 114. No studies of oxygen levels in cases showing clinical evidence of distress have been reported in the literature, but it has been shown that clinical "asphyxia" at birth is associated with very low oxygen levels (see page 25).

Three main conclusions can be drawn from the findings.

(a) At the time the foetus passes meconium, its oxygen supply is very poor. The saturation with oxygen is under 30 per cent.

(b) The foetus which passes meconium will, in most cases, have begun labour with an already deficient oxygen supply. The well oxygenated foetus has nearly 100 per cent. reserve of oxygen at term, enough to withstand the effects of most labours, and because of this the incidence of meconium staining at term is very low. After term, however, the incidence of meconium staining rises as the oxygen supply to the foetus falls and more

and more foetuses have, before labour, an oxygen supply approaching "distress levels" (see Fig. 56). By the 42nd and 43rd week, the supply may be so low that meconium may be passed without any stress of labour (see Case 11) and the incidence of meconium staining in labour becomes quite high. The incidence of meconium staining "unexplained" by difficult labour or other factors which might depress the oxygen supply is the same in all parities, as pregnancy becomes prolonged.

(c) The passage of meconium by the foetus is the first and often the only sign of uncomplicated anoxic anoxia. Meconium staining with very low oxygen levels (Case 11), or in the presence of extensive placental separation (Case 14), occurs alone and without slowing or irregularity of the foetal heart.

Foetal death from anoxia frequently follows a period during which the foetus passes meconium, and without any foetal heart abnormality preceding death (Cases 4, 6, 7, and 10).

Most previous investigators (pages 52 to 56) have been concerned with the state of the infant at birth. "Asphyxia" at birth is a complex clinical syndrome associated in many instances with traumatic delivery (e.g. 27 per cent. of breech deliveries, 25 per cent. of all operative deliveries, Lund, 1941), and therefore a degree of cerebral damage, and much less frequently with uncomplicated anoxia. Schwarz (1858) on clinical grounds alone

has also suggested that meconium staining is the first sign of uncomplicated anoxia.

After term, prolonged or difficult labour with mechanical pressure on the foetal head frequently complicates the clinical picture and meconium staining because of anoxia may frequently be accompanied by slowing or irregularity of the foetal heart because of pressure on the foetal head in the pelvis.

## (II) APPLICATION OF THE RESULTS TO THE CLINICAL PRACTICE OF OBSTETRICS.

### (1) Obstetric Death.

Figs. 60 and 61 and Tables XXIV to XXVII have shown that the obstetric death rate rises after the 40th week of pregnancy and that this rise is due mainly to an increase in rate of "unexplained" anoxic death, and of anoxic death in prolonged labour. After the 41st week, some 55 to 65 per cent. of all deaths are due to this cause. There is also a rise in incidence of deaths from birth trauma.

As pregnancy is prolonged after term, the oxygen supply to the foetus is deteriorating rapidly and is worse in some foetuses than others (Fig. 56), and some foetuses are likely to die because of oxygen deficiency alone ("unexplained" anoxic death). In some foetuses the oxygen supply even at term is insufficient to maintain life and the risk increases progressively with each week after term. A lesser degree of anoxia, insufficient to cause death of the foetus before labour, would predispose to death in prolonged labour, especially if inadequate or irregular contract-:ions interfered with placental blood flow (page 25). Anoxic death during or after prolonged labour is rare before the 40th week, but after the end of the 41st week is responsible for nearly 25 per cent. of all deaths. The rising incidence of

prolonged and difficult labour after term (Fig. 71) contributes greatly to this result - but more and more foetuses begin labour with a poor oxygen supply. It is not part of this thesis to discuss obstetrical treatment or suggest how such deaths may be prevented. Quantitative estimations of oxygen and statistical analysis of the effects of prolonged pregnancy on the incidence of obstetric death and of "foetal distress" lend support to those obstetricians who, on clinical grounds, have held that "post-maturity" is potentially dangerous. Nearly 60 per cent. of all obstetric deaths after the 41st week (Table XXVII) are due to anoxia alone and 25 per cent. to birth trauma. The already anoxic foetus is much less able to withstand the traumatic effects of difficult delivery and preceding anoxia contributes greatly to death in that 25 per cent. (see Case 8).

Clinical treatment based on an appreciation of the findings discussed can prevent death of many babies, and it is possible to reduce the obstetric death rate after 40 weeks by at least 60 per cent. by appropriate clinical measures (Walker, 1954).

(2) Meconium Staining of the Liquor Amnii.

The significance of this sign has been fully discussed. In clinical practice it should be accepted that when the foetus passes meconium, it is short of oxygen, even though its heart rate is regular and normal. Many infants will be born alive even when

the liquor has been stained with meconium for many hours, but where the depth of staining is increasing or the meconium is becoming lighter in shade (from higher in the bowel), the risk of anoxic death is becoming very great and the foetus may not survive unless rescued. The risk to such a foetus is greater if a further prolonged period of labour is to be expected, and especially if the mother is in the older age groups.

Slowing of the heart rate of the foetus which is already passing meconium is a particularly dangerous sign and suggests either that death is imminent, or that undue pressure on the foetal head is further damaging the already anoxic foetus.

(3) Use of Oxygen to the Mother.

Where meconium staining is seen and while delivery is awaited, oxygen by B.L.B. mask to the mother at 4 to 5 litres improves the oxygen supply to the foetus and is a worth while practice (see Discussion, p. 23; Walker, 1953).

(4) Pre-eclampsia.

The greatest risk to the foetus is in cases of "severe" toxaemia and especially in very young and rather old mothers. The problem is complicated, however, by the clinical finding that in many cases of severe pre-eclampsia, the foetus is very small and even if rescued by Caesarean Section it will die neonatally.

In other degrees of pre-eclampsia there may be little, if any, interference with the oxygen supply, but the risks of

"postmaturity" are greater if pre-eclampsia is also present (Case 4).

(5) Previous Obstetric Death.

If elective Caesarean Section or induction of labour is to be performed where the previous child was stillborn, the results suggest that some time between the 37th and 39th weeks of pregnancy should be selected for delivery. By the 37th week the foetus is usually sufficiently mature (See Fig. 72), and where obstetric death in the previous pregnancy has occurred earlier, the oxygen levels are likely to be deteriorating rapidly by this time. Where obstetric death has occurred, after term in previous pregnancies, the oxygen levels at 39 weeks will be still high, but beginning to fall. Induction at this time is often followed by short and easy labour in those cases with a child in excellent condition, and the necessity for elective Caesarean Section avoided.

(6) Anaesthesia.

In view of the wide variation in the oxygen levels in the blood of foetuses in clinically normal pregnancy between the 38th and 43rd weeks of gestation, the apparent effects of anaesthesia (pages 21 to 22) must be critically reviewed.

Anaesthesia to the mother may affect the foetus by lowering the per cent. saturation with oxygen of the maternal blood, decreasing the arterio-venous difference, alteration of uterine tone, interference with utero-placental circulation or histo-toxic

action on the cells of the placental membrane. Some of these effects will be specific to the anaesthetic, others will depend on how efficiently it is given. There is, at the moment, a swing away from the "simpler" to more complicated forms of anaesthetic. The effect of anaesthesia on the oxygen supply to the tissues of the recipient is unknown (Pask, 1953; McIntosh, 1953), and we have no knowledge of the effect of anaesthesia in general or of individual anaesthetics or mixtures of anaesthetics on the uterine tone, utero-placental circulation, or on the cells of the placental membrane.

Until those problems have been studied, the relative merits of various forms of anaesthesia in obstetrics cannot be discussed. In many cases the baby can be delivered within a few minutes of the start of the anaesthetic, in which case the effect on the foetus will be slight but maternal cyanosis during induction or prolonged inhalation of mixtures low in oxygen (for example, prolonged use of gas/air machine) must greatly diminish the supply of oxygen available to the foetus.

From information at present available it would appear that, for delivery of the already anoxic foetus, spinal, local or caudal anaesthesia is best as the oxygen supply to the foetus is unimpaired provided a drop in maternal blood pressure is avoided or quickly controlled.

## (III) SIGNIFICANCE OF THE RESULTS IN A STUDY OF THE PHYSIOLOGY OF THE FOETUS.

In the following paragraphs I have considered the findings of this research in relation to some aspects of the physiology of the foetus in utero. Much of this discussion is theoretical but is based on existing knowledge which is still imperfect.

### (1) Dissociation Curve of the Blood of the Human Foetus.

From a study of the findings in animal haemoglobin and bloods (pages 35 to 37), it would appear that in very early pregnancy the dissociation curve of foetal haemoglobin and blood is well to the left of the normal adult curve and hyperbolic in shape. As pregnancy progresses, the curve gradually approaches the adult curve until it is close to or within the adult range and is sigmoid to the adult extent. In one of the cases studied by Barcroft et al (1934), the curve of the kid at birth was indistinguishable from that of a non-pregnant adult goat. Despite the different characteristics of human foetal haemoglobin (page 36), the dissociation curve of human foetal blood seems to behave similarly to that of mammalian blood, although only a few studies are available (page 37; Figs. 20 and 22).

The position of the foetal curve has been attributed to the nature of foetal haemoglobin, and the change with advancing pregnancy to the gradual introduction of adult haemoglobin and not to alteration in pH of the blood (Barcroft, 1938). If the shape and

position of the dissociation curve of the foetus at term depends on the amount of adult haemoglobin present, then those foetuses with 10 per cent. adult haemoglobin (Fig. 57) must have a very different curve from those with 40 per cent.

Barcroft (1938) shows that in acclimatisation to altitude, production of extra haemoglobin has the effect (amongst others) of shifting the dissociation curve of the blood to the left, and compares the new position of the curve to the foetal or pre-natal curve. If increase in haemoglobin causes an alteration in the curve, then the foetus at term with a haemoglobin of 20 g. (stimulated by anoxia) must have a very different curve from the foetus with a haemoglobin of 15 g. per 100 ml.

Increased acidity of the blood causes a shift to the right of the dissociation curve (page 35). In the normal well oxygenated foetus the pH of the blood is 7.20, but in the anoxic foetus the pH is 7.04 (Eastman, 1932). The dissociation curves in the two foetuses must be very different.

The shape and position of the dissociation curve of the foetus at term must therefore vary over a wide range. Shifts in the dissociation curve must be of great importance to the individual foetus and must play a significant role in the respir-:atory exchange in utero, but no estimations have been made along those lines. A study of cases would need to be made firstly under the pH and carbon dioxide conditions existing in the blood at the

time and the haemoglobin level and adult/foetal haemoglobin percentages would need to be known. If such a study were made and correlated with the clinical features of the pregnancy, much would be learned of the respiratory mechanisms of the foetus, and especially of the tensions of oxygen available to the foetal tissues under normal and abnormal conditions.

(2) Environment of the Foetal Tissues.

At 40 weeks the blood reaching the foetus in the umbilical vein is at the best little over 60 per cent. saturated with oxygen, and that returning in the umbilical artery is about 30 per cent. saturated. Applying those saturations to the dissociation curve (Fig. 20), it is seen that the oxygen tensions are about 30 and 18 mm. of mercury respectively. The tension of the blood reaching the foetal brain and heart muscle is lower than that in the umbilical vein and may well be about 22 mm. of mercury (see Table XXXVII). At those levels, however, the foetus functions normally, due mainly to the low metabolic activity of the brain in utero.

If the per cent. saturation of the blood in the umbilical vein falls to 40 per cent. as it does by the 42nd week of gestation (and provided there is no shift in the dissociation curve with rising haemoglobin), the tension of oxygen in the blood reaching the brain and heart muscle will fall well below 20 mm. of mercury. At "distress" levels, the blood reaching the brain has an oxygen tension of around 15 mm. of mercury and that reaching half of the

body from the abdominal aorta must contain little or no oxygen.

Shifts in the curve due to rising haemoglobin will lessen the available oxygen in the carotid artery. Shifts to the right with anoxia will increase the tension available, but will lessen the ability of the foetus to take up oxygen from the mother. There must be a limit of oxygen tension below which the higher brain cells cannot maintain adequate function (especially near term when the oxygen demand is rising, see page 40), even though the foetus can remain alive.

(3) Anaerobic Metabolism.

Anaerobic metabolism of glucose produces energy for cerebral cells at the expense of a great increase in the production of lactic acid and a fall in the pH of the blood. This acid must be removed and glucose must be transported to the cells in high concentration. The cerebral circulation must therefore remain intact, (resistance of the foetus to ischaemic anoxia is no better than the adult). Under those conditions, an oxygen debt is built up and unless adequate oxygen becomes available within a relatively short time, death will occur. Anaerobic metabolism therefore appears to be an emergency measure of limited scope, called into play as a last resort. If Noguchi (1937) is correct, and the passage of meconium follows a fall in the pH of the blood, it may be true that the appearance of meconium follows the onset of anaerobic metabolism. This would seem a reasonable assumption as at distress levels the oxygen tension of the blood reaching the brain is at or

below 15 mm. of mercury.

At this level a certain amount of aerobic metabolism will still take place, but any further fall in oxygen tension with cerebral metabolism becoming completely anaerobic, must place the higher brain cells in great danger of irremediable damage, even though in some cases the foetus is ultimately born alive.

(4) Intra uterine relationships at or after Term.

Reynolds (1949) has attempted to define the intra uterine relationships in the late weeks of pregnancy and from his account it would appear that the steps are as follows:-

Increase in growth of the foetus with stretching of the uterine muscle and increasing tension in the uterine wall. This will lessen the utero-placental blood flow and will interfere with placental nutrition. Degeneration of the placenta causes alteration in its hormonal and chemical function and limits the production of hormones which have up to this time inhibited uterine contraction. Withdrawal of those hormones then allows the stretched and tense uterus, which is becoming more and more irritable, to respond to hormonal and chemical stimulation (of placental or other origin) and labour begins.

Reynolds goes on to state "the physiological conditions which set the stage for expulsion of the products of conception are also those conditions which impair the nutritive supply to the foetus. The effects, onset of labour and inadequate nutrition-:al supply for the embryo,are the result of a common cause, rather

than one a cause of the other."

This rather simple summary of an extremely complex problem would suggest that the primary factor is the growth of the foetus relative to the ability of the uterus to accommodate it by stretching. It would appear from this account that interference with utero-placental blood flow precedes, and is probably the cause of, placental syncitial degeneration. The fall in utero-placental blood flow lessens the oxygen available to the foetus. This effect is compensated for in some degree by the haemoconcentrat-:ion which occurs towards term (pages 15 to 16), so that each volume of maternal blood can carry a little more oxygen. Degen-:eration of the cells of the placental membrane would not necessarily interfere with the diffusion of oxygen, in fact thinning of the membrane might cause it to improve (Reynolds, 1949), and to some extent offset the effect of the falling blood flow. Withdrawal of placental inhibiting hormones could therefore allow labour to proceed when the oxygen supply to the foetus is still good (as normally occurs at term).

I have shown, however, that pregnancy proceeds beyond term in about 20 per cent. of cases (Table VIII), and that the oxygen supply falls rapidly even though the foetus continues to grow (Fig. 72). At term the transfer of diffusible nutrients to the foetus is much in excess of requirements (pages 30 to 31), but there is little reserve of oxygen, so that continued growth could still occur even though the oxygen supply might become extremely low.

It would appear, however, that in the postmature pregnancy, labour may fail to occur at a suitable time for the foetus because of some defect elsewhere in the chain of events, which normally precede the onset of "pains." The findings in Fig. 71 which demonstrate a great increase in uterine dysfunction of severe degree in labours after term, suggest that the initiation and maintenance of labour is inefficient in the postmature.

## (IV) ADVANCING MATERNAL AGE.

The older the mother at the time of first pregnancy, the more likely is the foetus to manifest distress in labour or to die of anoxia. In the primigravida under twenty, anoxic death of the foetus in late pregnancy (uncomplicated by pre-eclampsia) is uncommon, and even with pregnancy prolonged to the 43rd week, there is little increase in distress rates.

These findings suggest that in the young woman the vascular system of the uterus is able to adapt itself more easily to the demands of pregnancy, and to maintain an adequate oxygen supply even when the uterine circulation begins to fail in late pregnancy.

According to White ( 1951), the uterine arteries are the first to degenerate with age. It would seem reasonable to postulate that the uterine musculature and vascular system and the hormones of reproduction are designed for a functional life of some thirty years (15 to 45). If pregnancy occurs for the first time late in that period, hormonal balance and control is likely to be less accurate, muscle growth and stretching less efficient, and vascular growth limited. By this time, also, abnormalities, such as hypertension with permanent vascular changes, may have become superimposed.

Those theories might explain the clinical findings but no experimental studies are available of the effect of age on physiological function.

## (V) IMPORTANCE OF THE FINDINGS IN A STUDY OF THE LONG TERM EFFECTS OF ANOXIA.

The findings of this thesis make it possible to institute a long term follow up of infants known to have suffered serious anoxia. In a few cases, oxygen levels are available. In those where heavy meconium staining was present without foetal heart slowing or irregularity, it can be assumed that anoxia of severe degree was present without the complication of intra cranial damage due to pressure on the foetal head.

Previous investigations (page 47) have been either retrospective, or have not clearly distinguished infants who have suffered uncomplicated anoxia from those in whom a certain degree of cerebral damage might also have been present. After birth, the metabolic activity of the brain and presumably the demand for oxygen rises rapidly and the arterial blood is normally 80 per cent. saturated within half an hour of birth (Smith and Kaplan, 1942). A foetus may therefore suffer brain damage in the immediate post natal period if adequate respiration is not established quickly and a postnatal circulation established and maintained (page 44).

The findings of a careful study of this kind might alter the practice of obstetrics if it was shown that a long period during which the foetus was anoxic (passage of meconium) and living mainly by the anaerobic metabolism of glucose was detrimental to its future wellbeing.

In addition, the aetiology of various forms of spastic diplegia and other forms of mental retardation said to follow difficult birth might be more clearly defined (See Case 15).

(VI) OXYGEN SUPPLY IN EARLY PREGNANCY.

Table XI and Figs. 50 and 51 show that at the 21st to 22nd week the saturation with oxygen of the blood in the umbilical vein is 67 to 75 per cent. and the oxygen content is 12.4 to 14 vols. per cent. The haemoglobin (oxygen capacity) is just reading adult levels. At this time the placenta is little smaller than the foetus itself and I would have expected higher readings of percent saturation. It is suggested by Reynolds (1950) that there is a temporary interference with uterine blood flow about this time. Many more readings before and after this period would be necessary to establish the correct pattern. Opportunities to study the physiology of the normal placenta and foetus at this stage are few, but information must be sought. Gillespie (1950) suggests, for example, that normal growth of the foetus in late pregnancy depends in great part on adequate development of the myometrium and blood vessels in the first 20 weeks. The primary area of placenta differentiated (at 8 to 10 weeks) may, along with the amount of uterine stretching in late pregnancy, decide the ultimate size of the placenta and its ability to transfer nutrients to the foetus.

I have drawn only those conclusions which were justified by the findings themselves or when the findings were related to known physiological or clinical facts. I have preferred to leave unexplained many of the findings where only theoretical discussion based on inadequate evidence would have been possible.

Very few studies have been made on the human mother and foetus during normal pregnancy, partly because physiological experiments are difficult to design, and apply, where the integrity of the pregnancy must be maintained. Only by studies of the normal, however, can the obstetrician or the physiologist hope to assess the value of the multitude of observations of all kinds made on abnormal pregnancies.

The "normal" is difficult to define in human reproduction, but youth, optimal health, and clinically normal function should be taken as guides to cases selected for study.

A fertile field exists from which the human physiologist and the obstetrician together may reap a rich harvest.

## SUMMARY.

## PREFACE.

(1) Epidemiological study of the outcome of all pregnancies in a community can define population groups more liable to develop morbid states.

(2) Study of the aetiology of death of mature babies from anoxia showed that the risk was much greater if pregnancy was prolonged after term. This finding promoted a study of the oxygen supply to the human foetus.

## INTRODUCTION.

(A Review of the Literature)

(1) The oxygen levels in the blood of the umbilical vessels of the mammalian foetus show a wide scatter of results. It has been demonstrated, however, especially in the sheep foetus, that the oxygen supply undergoes a series of well ordered changes which can only be understood if the stage of gestation is known and the relations between oxygen capacity, oxygen content and percent saturation are considered at each stage.

(2) In the sheep, goat and rabbit foetus the percent. saturation of the blood in the umbilical vessels rises till after mid pregnancy, remains high till late pregnancy, but falls rapidly near term. In the rabbit it has been shown that this fall continues after term and the oxygen supply may become so low that the foetus dies.

(3) In the human foetus, readings taken before the onset of labour are few, and show a scatter of results, no pattern of changes has been demonstrated and no relation has been shown between capacity, content and percent saturation.

(4) The oxygen content of the blood in the umbilical vein of the human foetus after spontaneous delivery without anaesthesia has been shown by most observers to be a little over 10 vols. per cent. with a saturation of 45 to 50 per cent. The scatter of readings in each series is wide. No attempt has been made to assess the effects of difficult labour or abnormal pregnancy.

(5) The supply of oxygen available at the maternal side of the placenta is affected by -

(a) The percent saturation of the mother's blood, and the position and shape of the dissociation curve of the mother's blood.

(b) Rising maternal blood volume and increased cardiac output and by the fall in both which occurs towards term.

(c) The maternal systolic blood pressure and its relation to the intra uterine pressure.

(d) The volume of blood in the uterine circulation which rises during pregnancy, only to fall greatly towards term as the uterine wall becomes distended and tension in the wall rises.

(e) Anaesthetics given to the mother will, on the whole, depress the percent saturation with oxygen of the foetal blood. Spinal anaesthesia does not affect the foetus unless a marked fall in maternal systolic pressure occurs.

(f) Labour appears to depress the supply to a slight degree.

(6) The placenta in the human grows steadily during pregnancy but during the last few weeks there is only a very slight increase in size, associated with degenerative changes in cells of the placental membrane and histochemical changes in the villi.

(7) The rate of transfer (per unit weight of placenta) of diffusible nutrients from mother to foetus increases for the first nine-tenths of pregnancy and falls precipitously after that

time. The rate is uninfluenced by easy labour or anaesthesia but is depressed in pre-eclampsia.

(8) The uptake of oxygen by the foetal blood and the supply available to the foetal tissues is affected by -

(a) The haemoglobin level. In the last few weeks, in the sheep foetus, readings show a wide scatter, and in some cases the haemoglobin is much above normal adult levels due to an increased production of cells in response to the falling oxygen supply at this time.

(b) The dissociation curve of the foetal blood which varies throughout pregnancy both in position and shape but which at or near term, in the goat foetus, approaches the position and shape of the curve of the non-pregnant adult. The changes in the curve and its approach to the adult curve are due to varying proportions of adult and foetal haemoglobin in the blood each having a different affinity for oxygen.

(c) The demand of the foetus for oxygen which, in the last half of pregnancy in the sheep foetus, rises as the weight of the foetus rises. The demand increases very slowly in the later part of pregnancy since the daily increase in weight is small and varies from foetus to foetus as the scatter of weights at or near term is very great. A great variation also exists in the weights of human foetuses at or near term.

(d) The percent saturation of the blood reaching the foetal brain will vary with that of the blood in the umbilical vein, but is also lowered by dilution with blood of low saturation from the hind limbs and in the chambers of the heart. The details of the foetal circulation studied in the sheep have been confirmed to some extent by limited experiment in the human foetus.

(9) The foetus responds to anoxia -

(a) If slowly developing, by increasing the oxygen carrying capacity of its blood by the production of more red cells (sheep).

(b) If severe, by utilisation of an ability to metabolise glucose anaerobically. It may not, however, survive unharmed as significant mental damage has been reported in children who were severely asphyxiated at birth.

(c) If the higher cerebral centres are inhibited by anoxia, an inspiratory gasp may result by release of stimuli from primitive centres.

(10) Clinical syndromes related to anoxia.

(a) Anoxia is a frequent cause of stillbirth and early neonatal death, but in about 30 per cent. of cases no clinical reason can be found to explain why anoxia occurred. Unexplained anoxia is a common cause of death in postmature babies.

(b) "Foetal Distress" in labour is more common after the 40th week of pregnancy but opinion is divided as to whether slowing of the foetal heart rate or the passage of meconium is the most valuable prognostic sign of "asphyxia" of the foetus at birth.

(c) It is not known why an anoxic foetus should pass meconium but it is suggested that stimulation of the gut follows an alteration in carbon dioxide tension in the blood following a fall in pH.

## METHODS AND TECHNIQUES.

(1) Haemoglobin in cord blood of the foetus was measured by the M.R.C. Grey Wedge Photometer and the oxygen content by the micro technique of Roughton and Scholander (1943). A full discussion of the techniques and of problems in practical use is presented.

(2) Red cells were counted in a Neubauer counting chamber and the proportion of adult haemoglobin in the blood measured by an alkali denaturation technique (Jonxis, 1952).

(3) Blood samples, from a segment of umbilical cord, isolated between clamps immediately the child was delivered, were

aspirated anaerobically into syringes which were prepared, sealed, stored and transported as described by Roughton and Scholander (1943).

(4) Cases were studied provided full clinical details were available and the duration of pregnancy was accurately known. Where oxygen was to be estimated, spinal or local anaesthesia was employed, or the mothers were delivered without anaesthesia.

(5) Cases were classified normal, pre-eclampsia, threatened abortion earlier in the pregnancy, placenta praevia, previous stillbirth or early neonatal death, foetal distress, and the oxygen content was studied in addition in normal cases after spontaneous delivery and after difficult labour.

(6) Stillbirths and first week neonatal deaths (931 obstetric deaths) occurring in 23,461 booked cases in Aberdeen Maternity Hospital were studied in detail and classified in a new way, which is designed to ascribe the death to the clinical factor primarily responsible. There were nine groups in all, but deaths due to unexplained anoxia (in mature babies), anoxia under stress (prolonged labour), trauma (with the vertex presenting), and toxaemia are specially defined for study in the thesis.

(7) Cases of foetal distress occurring in 8816 booked cases were individually studied and a cause assigned to the distress in each case. Distress was then studied by total incidence, type (meconium or heart), and cause, in relation to parity, maternal age and duration of pregnancy.

## RESULTS.

(1) The haemoglobin level in the blood of the human foetus rises steadily till the 22nd to 24th week at which time it reaches normal adult levels, 14.8 to 15 g. per 100 ml. It may remain at that level till delivery, but after the 36th week there is a tendency for the levels to spread out and the mean level at each week of gestation rises steadily from 15.2 g. at the 38th week to 18.8 g. at the 43rd week. Readings as high as 18.6 g. may be found at the 40th week.

(2) The red cell count rises steadily throughout pregnancy and at the 40th week is 3.7 to 4.0 million per c.cm. when the haemoglobin is 14.8 to 15 g. and correspondingly higher with higher haemoglobin levels.

(3) Extra red cells are present and the haemoglobin level is higher than normal in pre-eclampsia, where abortion has threat-:ened earlier in the pregnancy, and when the foetus shows distress in labour.

(4) The oxygen content of the blood in the umbilical vein in normal pregnancy before the onset of labour falls from the 30th week at which time it is 14 vols. per cent till the 40th week when the highest reading is 12.7 vols. per cent. After this time the rate of fall is rapid till at the 43rd week the highest reading is 8.2 vols. per cent. The content in the artery parallels that in the vein and is 5 to 7 vols. per cent lower.

(5) The saturation with oxygen is 70 per cent at the 30th week, a maximum of 60 per cent at 40 weeks, and at 43 weeks is 30 per cent. The rapid fall in percent saturation after term is due to the marked rise in capacity which occurs as an excess of red cells is produced in response to the falling oxygen supply.

(6) There is an inverse correlation between the haemo-:globin reading (oxygen capacity) and the percent saturation with oxygen of the blood in the umbilical vessels. Haemoglobin readings over 16.5 g. are always associated with a saturation below 50 per cent. In clinically normal pregnancy at 40 weeks, even in live foetuses, saturation readings between 30 and 60 per cent may be found in the blood of the umbilical vein, but by 43 weeks the readings commonly range between 20 and 35 per cent.

(7) The percent saturation in the blood of the umbilical vein is unaffected in normal labour and in many cases of prolonged or difficult labour.

(8) When the foetus passes meconium the saturation with oxygen of the blood in the umbilical vein is at or below 30 per cent no matter the stage of gestation.

(9) The oxygen content and percent saturation are lower than normal in cases of pre-eclampsia, and in multigravidae in whom the previous pregnancy has ended with late abortion, still-birth or early neonatal death. In all such cases the oxygen capacity is much above normal for the stage of gestation.

(10) In the blood of the human foetus, adult type haemoglobin first appears at the 13th week. The proportion rises steadily but at term varies from 10 per cent to 40 per cent.

(11) Obstetric death of mature babies from causes clinically unexplained but with autopsy signs of anoxia is slightly more common in first pregnancies. Such deaths are much more likely in older primigravidae. Uncommon before the 40th week of pregnancy, they are seen increasingly more often as pregnancy becomes prolonged, and by the 43rd week are the most common type of obstetric death. They are responsible for 14.4 per cent of all obstetric deaths in primigravidae, and 12.8 per cent in multigravidae.

(12) Obstetric death from anoxia during or after prolonged labour is much more common in first labours because of the greater frequency of prolonged labour. Such deaths are much more likely in older primigravidae. Very uncommon before the 40th week of pregnancy, they are seen increasingly more often as pregnancy becomes prolonged, and by the 43rd week are, in primigravidae, responsible for nearly one-quarter of all deaths. They are responsible for 6.5 per cent of all obstetric deaths in primigravidae and only 1.7 per cent in multigravidae.

(13) Obstetric death from birth trauma during or after difficult labour is more common in first labours. Such deaths are much more likely in older primigravidae. They are seen at any time after the 38th week of pregnancy, but as pregnancy in primigravidae becomes prolonged, they occur more frequently. The proportion of deaths due to this cause by the 42nd week is 13.3 per cent., the same as at 40 weeks, but there are likely to be at least three times more deaths in the 42nd week. They are responsible for 7.5 per cent of all obstetric deaths in primigravidae, and 2.6 per cent in multigravidae.

(14) Obstetric death from toxaemia is directly related to the severity of the disease as judged by the degree of albuminuria. Somewhat more common in primigravidae, such

deaths are much more common the older the mother after the age of 20 (under 20 there is a high death rate). They are very uncommon after the 40th week of pregnancy, and they are responsible for about 10 per cent of all obstetric deaths.

(15) The foetus is much more likely to show "distress" in primigravidae and in difficult labours.

(16) In all parities the incidence of distress increases with rising maternal age and, in all parities, all age groups, and in all labours the incidence rises the longer pregnancy is prolonged after the 40th week.

(17) The rising incidence after the 40th week and with rising maternal age is due mostly to the increasingly frequent appearance of meconium.

(18) Distress without obvious clinical cause, and distress during prolonged labour, is mostly manifest by the passage of meconium, (often without any irregularity or slowing of the foetal heart).

(19) Distress due to undue pressure on the foetal head in the bony pelvis or if the head is held up on the perineum is usually manifest by slowing or irregularity of the foetal heart

without meconium staining.

(20) In multigravidae, unexplained meconium staining is seen just as frequently as in primigravidae. Foetal heart signs are uncommon in multigravidae because undue pressure on the foetal head is unusual and it is rarely held up by the perineum.

(21) The foetus, in primigravidae, will pass meconium in at least 17 per cent of labours at the 44th week, and in 20 per cent of all labours where the mother is over 35 years of age.

(22) The incidence of difficult labour rises steadily after the 40th week of pregnancy, and this rise is due mainly to an increase in the incidence of uterine dysfunction of severe degree.

## DISCUSSION.

(1) The experimental results are accurate, and the differences considered to be significant are well outwith the range of experimental error.

(2) There are two different factors responsible for the development of the blood picture normally seen in the foetus at birth. The first is the growth and maturation of the red cells and development of the oxygen carrying power of the blood.

At any time in the latter half of pregnancy an increase in the rate of red cell production may be superimposed on the growth pattern by the stimulus of anoxia.

(3) At 40 weeks the haemoglobin in the cord blood of the human foetus is 14.8 to 15 g. per 100 ml. and the red cell count about 4.0 million unless extra cells have been forced by anoxia.

(4) The scatter of haemoglobin and red cell readings found in the blood after the 36th week is due to individual variations in oxygen supply, and the lowest readings of haemoglobin and red cells are found in association with the highest oxygen levels.

(5) At term the oxygen supply to the well oxygenated foetus is good (12 vols. per cent in the vein) and there is nearly 100 per cent reserve for sudden emergency. The foetus can extract 6 to 7 vols. from each 100 ml. of blood, so long as that volume is present, as it has the ability to clear its blood of oxygen.

(6) Whenever the percent saturation falls much below 60 per cent (volume below 12 vols. per cent) there is, at any time after the 24th week, stimulation of red cell production. A minor fall in oxygen supply may be compensated by this means and the oxygen content may be kept at normal levels.

(7) If the supply of oxygen available at the placenta is further diminished, the content cannot be maintained, and the capacity rises steadily and the percent saturation falls rapidly, meconium staining appearing if the saturation falls below 30 per cent.

(8) In pre-eclampsia low oxygen levels compare with the poor rate of transfer of nutrients shown by other workers and are associated with early and severe placental syncitial degeneration, degenerative changes in utero decidual vessels and slowing of placental blood flow.

(9) Low oxygen readings following threatened abortion earlier in the pregnancy or where the previous pregnancy ended in death of the foetus, are not unexpected in the light of clinical experience, but no clear physiological explanation can be given.

(10) Oxygen levels found in the cord blood after spontaneous delivery are very similar to those found by other workers. They indicate that the infant born at or near term begins life with its blood at least 50 per cent saturated with oxygen and at the same percent saturation at which it was in utero before labour began.

(11) If the foetus begins labour with a good oxygen supply an adequate supply will be maintained in most cases, even in the presence of prolonged or difficult labour.

(12) At the time when the foetus passes meconium its oxygen supply is very poor. The foetus which passes meconium will probably have begun labour with an already lowered oxygen supply. Meconium is the first and only sign of uncomplicated anoxic anoxia in utero. Most previous investigators have complicated this discussion by considering "asphyxia neonatorum" which is a complicated clinical syndrome frequently due to trauma and only rarely to uncomplicated anoxia.

(13) The application of the results to the clinical practice of obstetrics is discussed and it is suggested that many obstetric deaths from anoxia could be avoided, especially those occurring after the 40th week of pregnancy.

(14) The significance of the passage of meconium is discussed with reference to obstetric care in labour, especially in the older mother or if labour is prolonged. Oxygen can be given to the mother as a therapeutic measure.

(15) In pre-eclampsia the clinical problem is complicated, since most foetuses which die are very small, and obstetric skill can rarely be brought to their rescue.

(16) Where elective delivery is considered in multigravidae with a history of obstetric death, the oxygen results indicate the best time for interference.

(17) Much of the previous work on the effect of anaes-:thesia must be reconsidered in view of the scatter of oxygen levels which may be found, even in normal foetuses at or near term. The effect of anaesthetics on the mother, the uterus, the utero-placental circulation, or the cells of the placental membrane is unknown, but the foetus is obviously endangered by the use of mixtures low in oxygen.

(18) The dissociation curve of the human foetus at term must vary over a wide range if it depends for its shape and position on the proportion of adult haemoglobin, the haemoglobin level and the pH of the blood.

(19) The foetal tissues must be able to survive at very low oxygen tensions in utero. Anaerobic metabolism is an emergency measure brought into play when the tension of oxygen in the blood reaching the brain cells falls too low. Meconium staining is probably clinical evidence that anaerobic metabolism (at least in part) has begun.

(20) The relationships in the uterus at or after term are discussed. Oxygen supply to the foetus is normally maintained by compensating mechanisms despite the fall in utero-placental blood flow which promotes syncitial degeneration. Occasionally labour may fail to occur in time to rescue the foetus before the oxygen supply is dangerously low.

(21) The detrimental effect of rising maternal age is probably related to an inadequate response of blood vessels and myometrium to the stimulation of pregnancy.

(22) The findings make it possible to institute a study of the long term effects of anoxia, since cases can be selected where anoxic anoxia was present uncomplicated by birth trauma.

(23) The oxygen supply in early pregnancy depends on factors at present imperfectly understood. No clear pattern emerges from a study of the findings.

## REFERENCES.

ABRAMSON, D.I., FLACHS, K. and FIERST, S.M. (1943)
Am. J. Obstet. Gynec. 45, 666.

d'AVIGNON, M. and KEILSON, I. (1953)
Acta Paediat. 42, 407.

BAIRD, D. and WALKER, J. (1954)
Chapter on Stillbirth, British Obstetric Practice. Heinemann, London.

BAIRD, D., WALKER, J. and THOMSON, A.M. (1954)
J. Obstet. Gynaec. Brit. Emp. (in press)

BARCLAY, A.E., FRANKLIN, K.J., and PRICHARD, M.M.L. (1946)
"Foetal Circulation," Blackwell, Oxford.

BARCROFT, J. (1925) Respiratory Function of the Blood.
Cambridge. Part 1, App.1. p. 182.

BARCROFT, J. and ROTHSCHILD, P. (1932)
J. Physiol. 76, 447.

BARCROFT, J., HERKEL, W. and HILL, R.M. (1933)
J. Physiol. 77, 194.

BARCROFT, J., ELLIOT, R.H.E., FLEXNER, L.B., HALL, F.G., HERKEL, W., McCARTHY, E.F. McCLURKIN, T., and TAALAT, M. (1934)
J. Physiol. 83, 192.

BARCROFT, J., FLEXNER, L.B. and McCLURKIN, T. (1934b)
J. Physiol. 82, 498.

BARCROFT, J., FLEXNER, L.B., HERKEL, W., McCARTHY, E.F. and McCLURKIN, T. (1935) J. Physiol. 82, 215.

BARCROFT, J., KRAMER, K., and MILLIKAN, G.A. (1937)
J. Physiol. 90, 18.

BARCROFT, J. (1938) Features in the Architecture of Physiological Function. Cambridge, p. 217-220.

BARCROFT, J., BARRON, D.H., COWIE, A.T. and FORSHAM, P.N. (1938)
J. Physiol. 97, 338.

BARCROFT, J. and KENNEDY, S.A. (1939)
J. Physiol. 95, 173.

BARCROFT, J., KENNEDY, S.A., and MASON, M.F. (1939a)
J. Physiol. 95, 269.

BARCROFT, J., KENNEDY, S.A., and MASON, M.F. (1939b)
J. Physiol. 97, 347.

BARCROFT, J. (1945) J. Physiol. 32 P.

BARCROFT, J. and YOUNG, I.M. (1945)
J. Exp. Biol. 21, 70.

BARCROFT, J. and ELSDEN, S.R. (1946)
J. Physiol. 105, 25.

BARCROFT, J. (1946) Researches on Prenatal Life.
Blackwell, Oxford.

BARTHOLOMEW, R.A. and KRACKE, R.L. (1932)
Amer. J. Obstet. Gynec. 24, 797.

BATTEN, D.H. (1943) Curr. Res. Anaesth. 22, 143.

BEAVEN, G.H., HOCH, H. and HOLIDAY, E.R. (1951)
Biochem. J. 49, 374.

BECKER, R.F., WINDLE, W.F., BARTH, E.E. and SCHULZ, M.D. (1940)
Surg. Gyn. Obstet. 70, 603.

BERUTI, J.A. and ROUST, A. (1948)
El. Dia Medico. 20/63. 2429-2440.

BLAIR-BELL, W., CUNNINGHAM, I., JOWETT, M., MILLET, H. and BROOKS, J. (1928) Brit. Med. Journ. I, 126.

BOOTHBY, W.M. (1938) Proc. Staff Meeting, Mayo Clinic, 53, 641.

BRINKMAN, R., WILDSCHUT, A. and WITTERMANS, A. (1933)
J. Physiol. 80, 377.

BRINKMAN, R. and JONXIS, J.H.P. (1937)
J. Physiol. 88, 162.

BRINKMAN, R. and WILDSCHUT, A.J.H. (1938)
Acta. Med. Scan. 94, 459.

BRINKMAN, R. (1953) Anoxia of the Newborn Infant.
Blackwell, Oxford. p. 125 and p. 219.

BROWNE, J.C. McC. and VEALL, N. (1953)
J. Obstet. Gynaec. Brit. Emp. 60, 142.

BUMM, E. (1893) Arch. f. Gynäk, 43, 181.

BURWELL, C.S. (1938) Amer. J. Med. Sci. 195, 1.

CALDEYRO-BARCIA, R. and ALVAREZ, H. (1952)
J. Obstet. Gynaec. Brit. Emp. 59, 646.

CALKINS, L.A. (1937) Amer. J. Obstet. Gynec. 30, 280.

CARLYLE, A. (1948) J. Physiol. 107, 355.

CATON, W.L., ROBY, C.C., REID, D.E., CASWELL, R., MALETSKOS, C.J., FLUHARTY, R.G. and GIBSON, J.G. (1951)
Amer. J. Obstet. Gynec. 61, 1207.

CHRISTOFFERSEN, A.K. (1934)
Compt. rend. Soc. de Biol. Paris. 117, 641.

CLAYTON, S.G. (1941) J. Obstet. Gynaec. Brit. Emp. 48, 450.

CLAYTON, S.G. (1953) Proc. Roy. Soc. Med. 46, 91.

COHNSTEIN, J. and ZUNTZ, N. (1884)
Pflug. Arch. ges Physiol. 34, 173.

COMROE, J.H. and BOTHELO, A.B. (1947)
Amer. J. Med. Sci. 214, 1.

COX, L.W. and CHALMERS, T.A. (1953)
J. Obstet. Gynaec. Brit. Emp. 60, 203.

CRUICKSHANK, J.N. (1930)
Med. Res. Council, Special Report Series 145.

DARKE, R.A. (1944) J. Paediat. 24, 148.

DARLING, R.S., SMITH, C.H., ASMUSSEN, E. and COHEN, F.M. (1941)
J. Clin. Invest. 20, 739.

DE LA MOTTE (1655 - 1737) Quoted by SCHULZE, 1925.

DE LEE, J.B. and GREENHILL, J.P. (1947)
Principles and Practice of Obstetrics.
9th Edition. Saunders, Philadelphi.

DE MARSH, Q.B., ALT, H.L., WINDLE. W.F. (1941)
J. Amer. Med. Ass. 116(2), 2568.

DIECKMAN, W.J. and WEGNER, C.R. (1934)
Arch. Int. Med. 53, 71.

DIECKMAN, W.J. and KRAMER, S. (1944)
Proc. Soc. Exp. Biol. and Med. 55, 242.

DRABKIN, D.L. and AUSTIN, J.H. (1936)
J. Biol. Chem. 112, 105.

DUNHAM, E.C. (1948) Premature Infants.
Washington. Child Bureau Pub. No. 325.

EASTMAN, N.J. (1930) Bull. Johns Hopkins Hosp. 47, 221.

EASTMAN, N.J. (1932) Ibid. 50, 39.

EASTMAN, N.J., GELLING, E.M.K. and DELAWDER, A.M. (1933)
Bull. Johns Hopkins Hosp. 53, 246.

EASTMAN, N.J. and McLANE, C.M. (1930)
Bull. Johns Hopkins Hosp. 47, 261.

FALKINER, N.M. and APHTHORPE, J.O.E. (1944)
J. Obstet. Gynaec. Brit. Emp. 51, 30.

FLEXNER, L.B. and GELLHORN, A. (1942)
Amer. J. Obstet. Gynec. 43, 965.

FLEXNER, L.B., COWIE, D.B., HELLMAN, L.M., WILDE, W.S., and VOSBURGH, G.J. (1948)
Amer. J. Obstet. Gynec. 55, 469.

FREED, F.C. (1927) Amer. J. Obstet. Gynec. 14, 659.

GIBBERD, G.F. (1952) New Zealand Med. J. 51, 277.

GIBSON, J.R. and McKEOWN, T. (1950)
Brit. Journ. Soc. Med. 4, 221.

GILLESPIE, E.C. RAMSEY, E.M. and REYNOLDS, S.R.M. (1949)
Amer. J. Obstet. Gynec. 58, 758.

GILLESPIE, E.C. (1950) Amer. J. Obstet. Gynec. 59, 949.

GLASS, H.G., SNYDER, F.F. and WEBSTER, F. (1944)
Amer. J. Physiol. 140, 609.

GOLDBLOOM, A. and GOTTLEIB, R. (1930)
J. Clin. Invest. 9, 139.

GUEST, G.M., BROWN, E.W., and WING, M. (1938)
Amer. J. Dis. Child. 56, 529.

HALDANE, J.S. (1920) J. Path. Bact. 23, 443.

HALL, F.G. (1934) J. Physiol. 80, 502.

HALL, F.G. (1935) Ibid. 83, 222.

HAMILTON, H. (1949) J. Obstet. Gynaec. Brit. Emp. 56, 548.

HAMILTON, W.J., BOYD, J.D. and MOSSMAN, H.W. (1945)
Human Embryology. Cambridge.

HAMILTON, W.J. and BOYD, J.D. (1951)
Proc. Roy. Soc. Med. 44, 489.

HASELHORST, G. and STROMBERGER, K. (1930)
Ztschr. f. Geburtsh. v. Gynäk. 98, 49.

HASELHORST, G. and STROMBERGER, K. (1931)
Ztschr. f. Geburtsh. v. Gynäk. 100, 48.

HAUROWITZ, F. (1930) Hoppe. Zeyl. Z. 186, 141.

HAUROWITZ, F. (1935) Ibid. 232, 125.

HELLMAN, L.M., FLEXNER, L.B., WILDE, W.S., VOSBURGH, G.J. and PROCTOR, N.K. (1948) Amer. J. Obstet. Gynec. 56, 861.

HELLMAN, L.M., HARRIS, B.A., and ANDREWS, M.C. (1950)
Bull.Johns Hopkins Hosp. 87, 203.

HELSTROM, B. and JONSSON, B. (1953)
Acta Paediat. 42, 398.

HERTIG, A.T. and ROCK, J. (1941) Contr. Embryol. Carneg. Inst. 29.

HERTIG, A.T. and ROCK, J. (1945) Ibid. 31.

HERTIG, A.T. and ROCK, J. (1949) Ibid. 33.

HILL (1935) Quoted by BARCROFT, J. (1946)

HIMWICH, H.E., ALEXANDER, F.A.D., and FAZEKAS, J.F. (1941)
Amer. J. Physiol. 133, 327.

HUGGETT, A.St. G. (1927) J. Physiol. 62, 373.

JONES, J.M., SHIPP, M.E. and GONDER, T.A. (1936)
Proc. Soc. Exp. Biol. et Med. 34, 873.

JONXIS, J.H.P. (1949) Haemoglobin, p. 261.
Butterworth, London.

JONXIS, J.H.P. (1952) Personal Communication.

JOPE, H.M. and O'BRIEN, J.R.P. (1949)
Haemoglobin, p. 269.
Butterworth, London.

KAISER, I.H. and CUSHNER, I.M. (1951)
Amer. J. Obstet. Gynec. 62, 6.

KARN, M.N. and PENROSE, L.S. (1951)
Annals of Eugenics. 16, 147.

KENNEDY, J.A. and CLARK, S.L. (1942)
Amer. J. Physiol. 136, 140.

KING, E.J. (1947) Biochem. J. 41, 32.

KING, E.J., GILCHRIST, M., WOOTTON, I.D.P., DONALDSON, R., SISSON, R.B. MacFARLANE, R.G., JOPE, H.M., O'BRIEN, J.R.P., PATERSON, J.M. and STRANGEWAYS, D.H. (1948a) Lancet, ii, 563.

KING, E.J., WOOTTON, I.D.P., DONALDSON, R., SISSON, R.B. and MacFARLANE, R.G. (1948b) Lancet, ii, 971.

KNAPPE (1897) Quoted by SCHULZE, 1925.

KOBBER, E. (1866) Inaug. Dissertation Dorpat.

LANDAIS (1892) quoted by GRASSET, J., LEVY, J., SEGAL,A., and PIALOUX, J. (1949)
Bull de l'Assoc. des Gynecol. et Obstet. 1/Suppl. 2, 125.

LATTO, D. (1951) Brit. Med. Journ. i, 1346.

LIEBSON, R.G. LIKHNITZKY,I.I. and SAX, M.G. (1936)
J. Physiol. 87, 97.

LIND, J. (1953) Anoxia of the Newborn Infant.
Oxford. p. 171.

LUND, C.J. (1940) Amer. J. Obstet. Gynec. 40, 946.

LUND, C.J. (1941) Ibid. 41, 934.

McCARTHY, E.F. (1943) J. Physiol. 102, 55.

McCLURE, R.D., BEHRMANN, V.G., and HARTMAN, F.W. (1948) Annals Surg. 128, 185.

McCUTCHEON, F.H. (1936) J. Cell Comp. Physiol. 8, 63.

MacFARLANE, R.G., WOOTTON, I.D.P., GILCHRIST, M. (1948) Lancet, i, 282.

McGREGOR, A.R. (1946) Brit. Med. Bull. 4, 174.

McINTOSH, R.R. (1953) Personal Communication.

McKEOWN, T. and GIBSON, J.R. (1952) Brit. Med. Journ. i, 938.

McKIDDIE, J.M. (1949) J. Obstet. Gynaec. Brit. Emp. 56, 386.

McLENNAN, C.E. and THOUIN, L.G. (1948) Amer. J. Obstet. Gynec. 55, 189.

McQUISTON, W.O., CULLEN, S.C. and COOK, K. (1943) Anaesthesiology. 4, 145.

MASTERS, M. and CLAYTON, S.G. (1940) J. Obstet. Gynaec. Brit. Emp. 47, 437.

MAYER, M. (1953) Anoxia of the Newborn Infant. Oxford. p. 1.

MILLER, J.R., KEITH, N.M., ROWNTREE, L.G. (1915) J. Amer. Med. Ass. 64, 779.

MORRISON, J.E. (1952) Foetal and Neonatal Pathology, London.

MUGRAGE, E.R. and ANDRESEN, M.I. (1936) Amer. J. Dis. Child. 51, 775.

NAEGELE, H.F. (1838) Die Geburtschülfleche Auskultatin. Mainz.

NEEDHAM, J. (1942) Biochemistry and Morphogenesis. Cambridge.

NELSON, T.R. (1954) Trans. Obstet. Soc. Edin. (In press)

NOGUCHI, M. (1936) Jap. J. Obstet. Gyn. 19, 328.

NOGUCHI, M. (1937) Ibid. 20, 248.

NOGUCHI, M. (1937b) Ibid. 20, 218, 358.

OETTINGER, L. and MILLS, W.B. (1949)
J. Paediat. 35, 362.

ORCUTT, F.S. and WATERS, R.M. (1937)
J. Biol. Chem. 117, 509.

PAGE, E.W. (1948) Obstet. and Gyn. Survey, 3, 615.

PASK, E.A. (1953) Personal Communication.

PONDER, E. and LEVINE, P. (1949)
Blood. Vol. 4, 1264.

POTTER, E.L. and ADAIR, F.L. (1943)
Amer. J. Obstet. Gynec. 45, 1054.

RAMSEY, E.M. (1949) Contrib. Embryol. 218.
Carnegie Inst. of Washington.
Pub. No. 583, 33, 113.

RATHBURN, L.S. (1943) Amer. J. Obstet. Gynec. 46, 278.

REENKOLA, M. (1948) Acta Obstet. Gyn. Scand. 28/Suppl. 3
(7 - 100)

REYNOLDS, S.R.M. (1949) Physiology of the Uterus (2nd Ed.)
New York. Hoeber.

REYNOLDS, S.R.M. (1950) Amer. J. Obstet. Gynec. 59, 529.

ROOS, J. and ROMIJIN, C. (1938)
J. Physiol. 92, 249.

ROSCOE, M.H. and DONALDSON, G.M.M. (1946)
J. Obstet. Gynaec. Brit. Emp. 53, 527.

ROUGHTON, F.W.W. and SCHOLANDER, P.F. (1943)
J. Biol. Chem. 148, 541.

ROUGHTON, F.W.W. (1952) Personal Communication.

ROVENSTEINE, E.A., ADRIAN, J. and STUDDIFORD, W.E. (1940)
Calif. and West Med. J. 53, 144.

SACHS, M.G. and LIKHNIZKAYA, I.I. (1938)
Bull de Biol. et de Medicine Exp. de
l'U.R.S.S. 5, 523.

SCAMMON, R.E. and CALKINS, L.A. (1929)
The Development and Growth of External
Dimensions of the Human Body in the Fetal
Period. Minneapolis. (University of Minnesota
Press).

SCHULZE, M. (1925) Amer. J. Obstet. Gynec. 10, 83.

SCHWARZ (1858) Quoted by SCHULZE, 1925.

SHAW, J.L. and DOWNING, V. (1935)
J. Biol. Chem. 109, 405.

SHAW, J.L., STEELE, B.F. and LAMB, C.A. (1937)
Arch. Surg. 35, 1.

SMITH, C.A. (1939) Surg. Gynaec. Obstet. 69, 584.

SMITH, C.A. (1945) Physiology of the Newborn Infant.
Illinois.

SMITH, C.A. and KAPLAN, E. (1942)
Amer. J. Dis. Child. 64, 832.

SNYDER, F.F. and GEILING, E.M.K. (1943)
Amer. J. Obstet. Gynec. 45, 604.

SNYDER, F.F. (1944) Anat. Rec. 88, 457.

SNYDER, F.F. (1949) Obstetric Analgesia and Anaesthesia.
Philadelphia. p. 148.

SOLLMAN, T. (1936) Manual of Pharmacology. Ed. 5.
Philadelphia. Saunders.

SPANNER, R. (1935) Z. ges Anat. Entwgsch. 105, 163.

STEEL, A.G. and WINDLE, W.F. (1938)
J. Physiol. 94, 525.

STEWART, D.B. (1952) J. Obstet. Gynaec. Brit. Emp. 59, 641.

STEWART, H.L. (1952b) J. Amer. Med. Ass. 148, 1079.

STIEVE, H. (1940) Quoted by Hamilton and Boyd, 1951.

STIEVE, H. (1942) Quoted by Hamilton and Boyd, 1951.

STIEVE, H. (1948) Quoted by Hamilton and Boyd, 1951.

TAYLOR, E.S., GOVAN, C.D. and SCOTT, W.C. (1951)
Amer. J. Obstet. Gynec. 61, 840.

TENNEY, B. (1936) Amer. J. Obstet. Gynec. 31, 1024.

TENNEY, B. and PARKER, F. (1940)
Amer. J. Obstet. Gynec. 39, 100.

THOMSON, A.M. (1949) J. Obstet. Gynaec. Brit. Emp. 56, No. 2.

THOMSON, A.M. (1951) Brit. J. Nut. 5, 158.

THOMSON, K.J., HIRSHEINER, A., GIBSON, J.G., and EVANS, W.A. (1938)
Amer. J. Obstet. Gynec. 36, 48.

VAN LIERE, E.J. (1942) Anoxia. Chicago. p. 173.

VAN SLYKE, D.D. and NEILL, J.M. (1924)
J. Biol. Chem. 61, 523.

WALKER, J. (1953) Chapter, Anoxia of the Newborn Infant.
Oxford. p. 158.

WALKER, J. (1954) Foetal Anoxia. (The Blair-Bell Memorial Lecture, September, 1953).
J. Obstet. Gynaec. Brit. Emp. (in press).

WATTS, J., HENDERSON, H., KAUMP, D.H., and DAVIS, R.M. (1951)
Amer. J. Obstet. Gynec. 61, 1025.

WAUGH, T.R., MERCHANT, F.T. and MAUGHAN, G.B. (1939)
Amer. J. Med. Sci. 198, 646.

WEGELIUS, R. (1948) Acta Paediat. 35 Suppl. 4.

WHITE, P. (1951) Amer. J. Obstet. Gynec. 61A, 382.

WILLIAMS, E.A. (1952) J. Obstet. Gynaec. Brit. Emp. 59, 635.

WILSON, R.A. TORREY, M.A. and JOHNSON, K.S. (1937)
Surg. Gynaec. Obstet. 65, 601.

WINDLE, W.F. (1940) Physiology of the Foetus.
W.B. Saunders, Philadelphia and London.

WINDLE, W.F. and BISHOP, C.L. (1939)
Proc. Soc. Exp. Biol. 40, 2.

WINTROBE, M.M. and SHUMACKER, H.B. (1935)
J. Clin. Invest. 14, 837

WINTROBE, M.M. and SHUMACKER, H.B. (1936)
Amer. J. Anat. 58(2), 313.

WISLOCKI, G.B. and DEMPSEY, E.W. (1946)
Endocrinol. 38, 91.

WISLOCKI, G.B. DEMPSEY, E.W. and FAWCETT, D.W. (1948)
Obstet. Gynaec. Survey. 3, 604.

WOOD, E.H., GERACI, J.E., and GROON, D.L. (1948)
Fed. Proc. 7, 137.

WOOD, E.H. (1950) Proc. Staff Meet. Mayo Clinic. 25, 384.

WOODBURY, R.A., HAMILTON, W.F. and TORPIN, R. (1938)
Amer. J. Physiol. 121, 640.

YOUNG, J. (1914) J. Obstet. Gynaec. Brit. Emp. 26, 1.

ZEEK, P.M. and ASSALI, N.S. (1950)
Amer. J. Clin. Path. 20, 1099.

ZEISEL, H. (1951) Ztschr. Kinder Heilk. 70, 190.

THE OXYGEN SUPPLY TO THE HUMAN FOETUS

and the Clinical Syndromes associated with Anoxia.

## APPENDIX.

(1) Diagrams and Illustrations.

(2) Tables.

(3) Illustrative Clinical Case Histories.

(4) Publications.

(1) DIAGRAMS AND ILLUSTRATIONS.

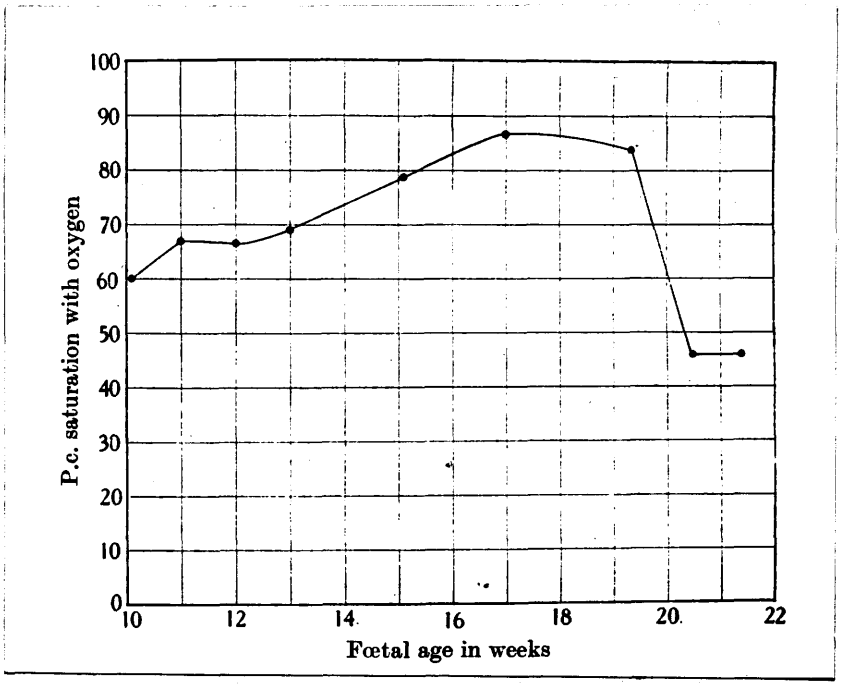



Fig. 1. Superior limit of estimations of percentage saturation of blood of the umbilical vein in the goat foetus. (Barcroft et al, 1934).

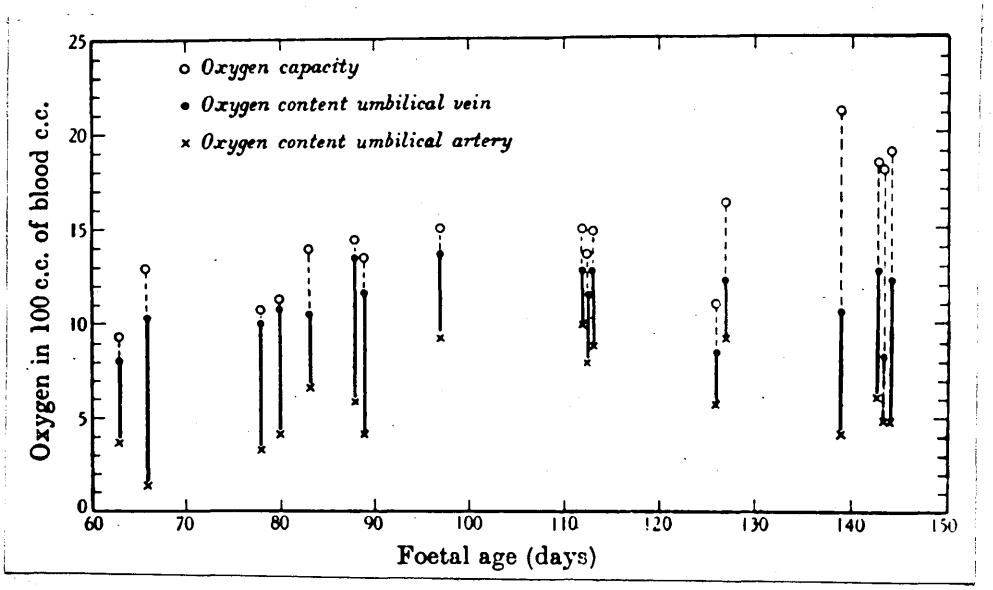



Fig. 2. Oxygen capacity and oxygen content of blood in the umbilical vessels during foetal life in the sheep. (Barcroft et al, 1939b)

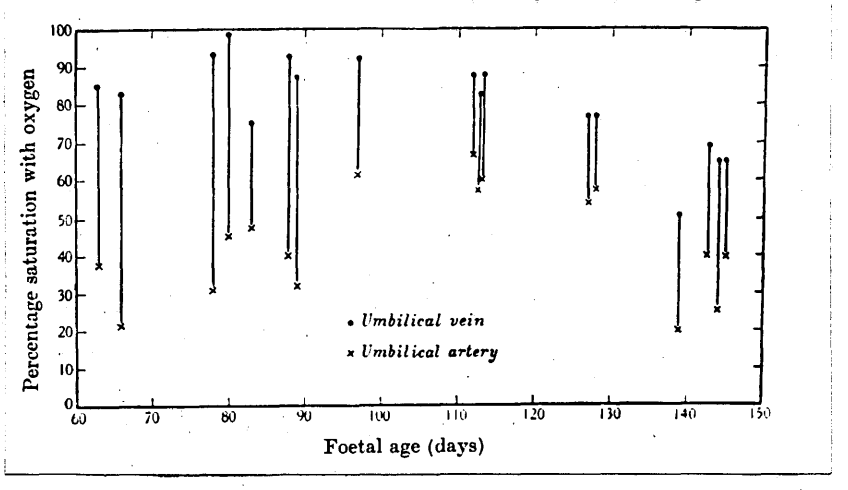



Fig. 3. Percentage saturation with oxygen of blood in the umbilical vessels during foetal life in the sheep. (Barcroft et al, 1939b)

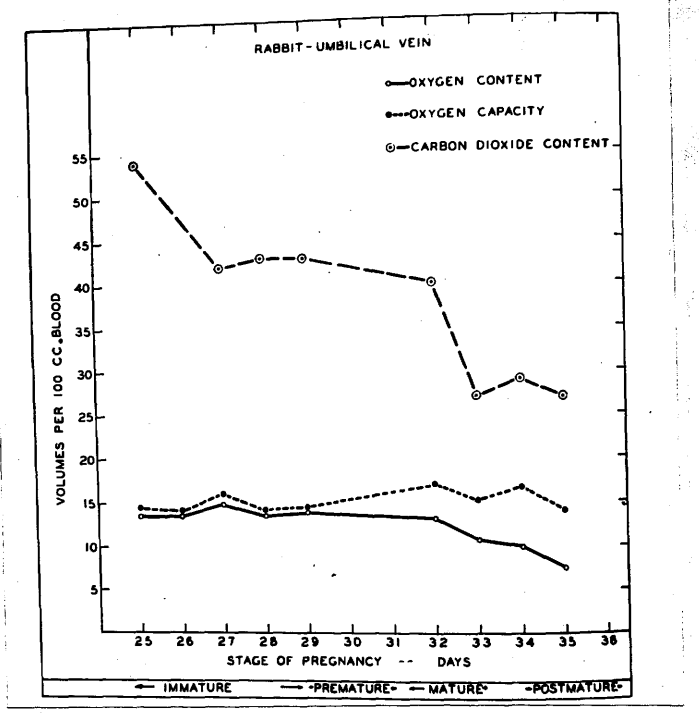



Fig. 4. Average oxygen capacity, average oxygen content and carbon dioxide content of the umbilical vein blood in the foetal rabbit. (Snyder, 1949)

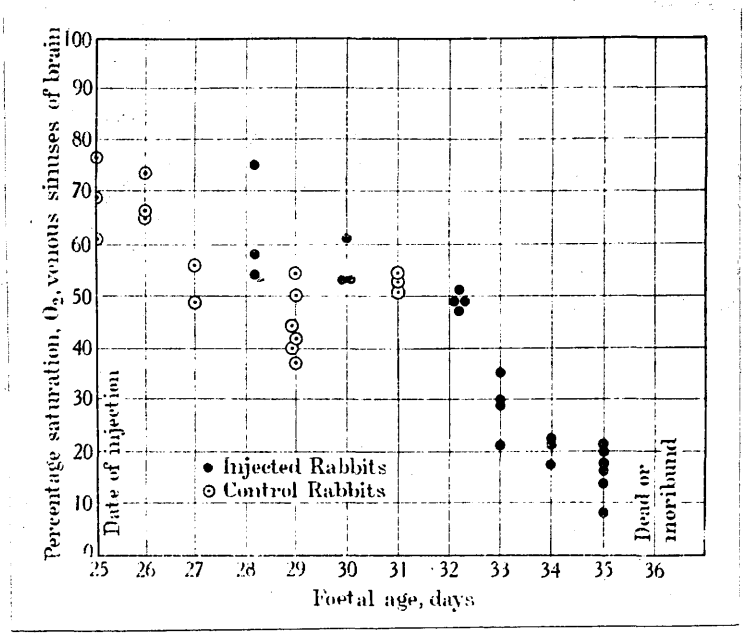



Fig. 5. Percent. saturation of blood in the cerebral venous sinuses of postmature rabbits. (Barcroft and Young, 1945)

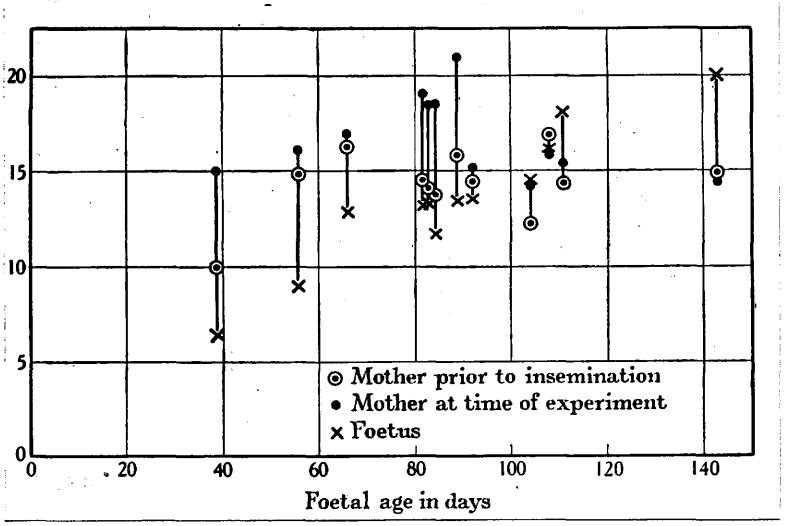



Fig. 6.
Oxygen capacity of blood of ewes before insemination and at time of giving birth to lambs.
(Barcroft, 1946)

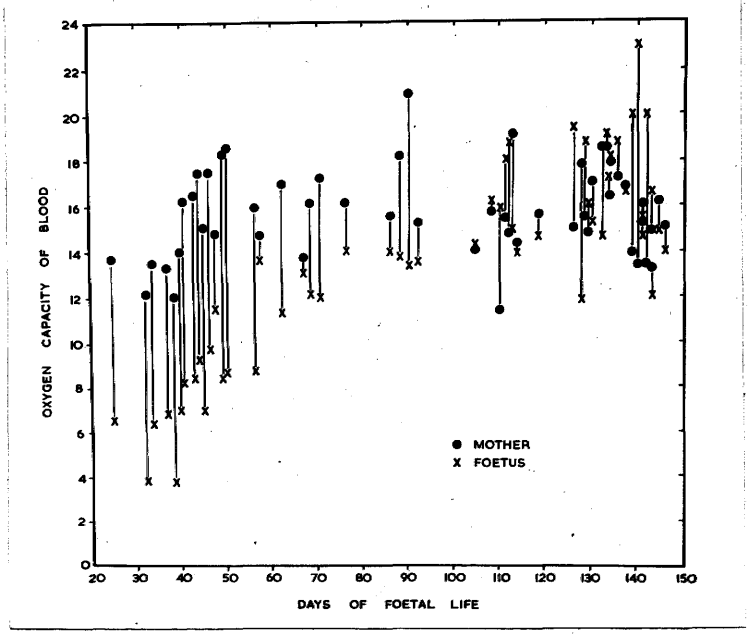



Fig. 7.
Oxygen capacity of blood of foetal sheep and of the mother's at successive foetal ages.
(after Barcroft, 1946)

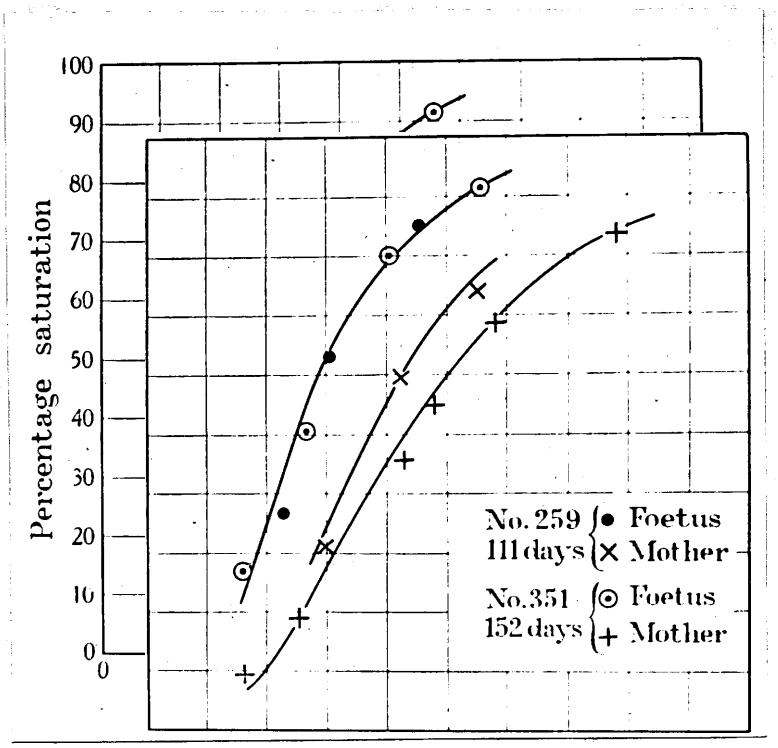
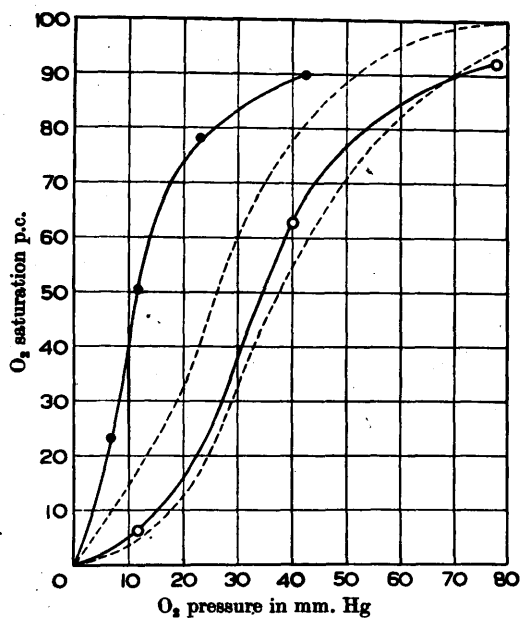



Fig. 8.
Dissociation curve of the blood of two pregnant sheep and of the foetuses. (Barcroft, 1946)




Cow pregnant about 8 months. (o) Maternal blood, (•) fœtal blood.
$CO_2$ pressure 43–45 mm. Hg. Temp. 38·5° C.

Fig. 9.
Dissociation curve of the blood of a pregnant ox at eight months of gestation and of the foetus. (Roos and Romijin, 1938)

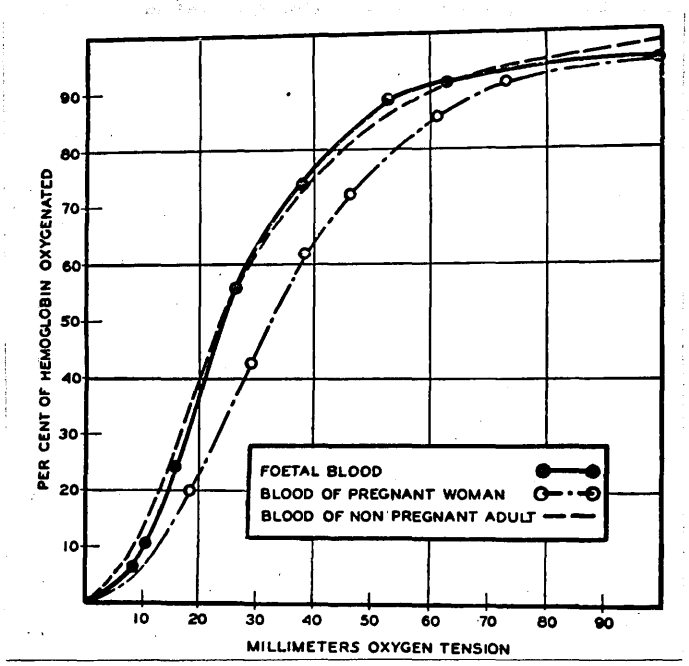



Fig. 10.
Dissociation curve of human maternal and foetal blood. (Eastman et al, 1933)

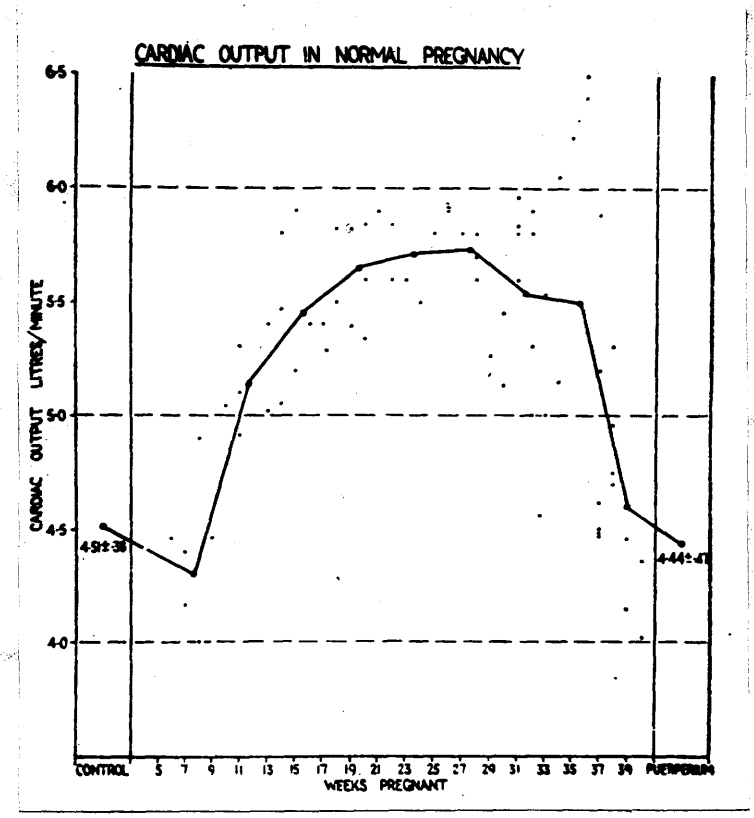



Fig. 11.
Cardiac output in normal human pregnancy. (Hamilton, 1949)

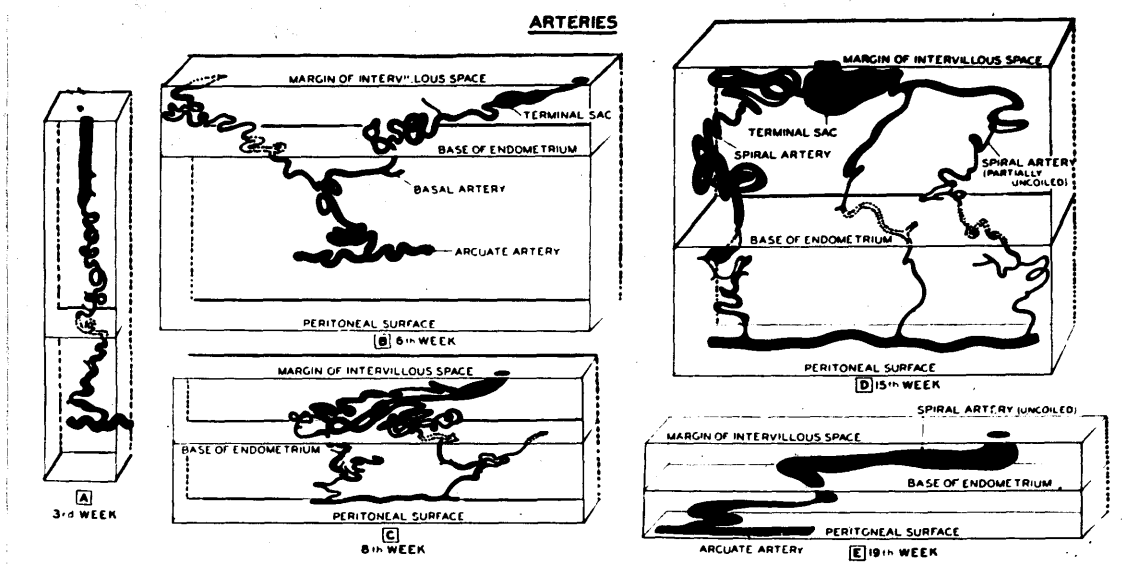



Fig. 12.
Diagram of the arrangements of the uterine arteries at the placental site of the pregnant monkey at various stages of gestation. (Ramsey, 1949)

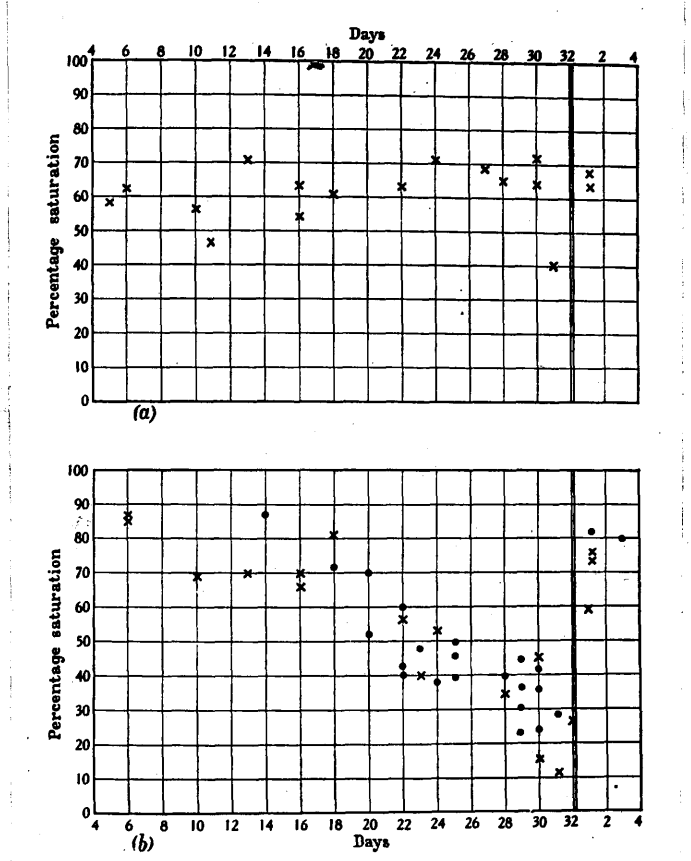



Fig. 13.
Percent. saturation of the blood emerging from (a) the non-pregnant and (b) the pregnant horn of the rabbit uterus. (Barcroft et al, 1935)

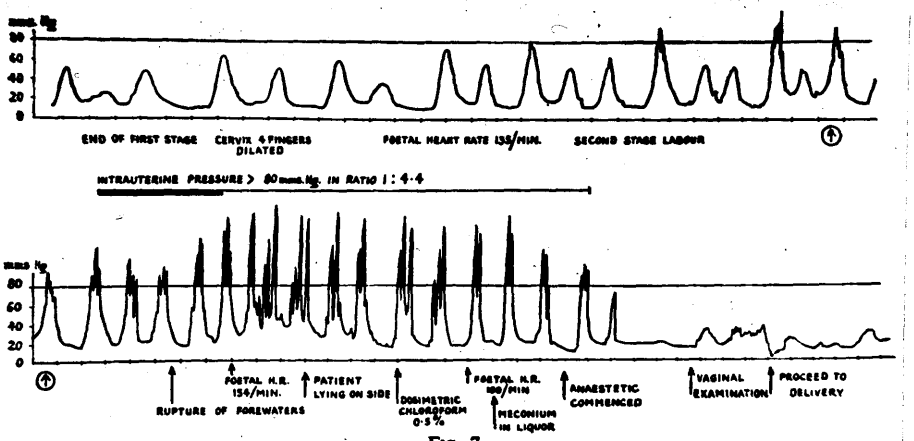



FIG. 7

Mrs. M., aged 23, para 1. A violent second stage of labour, with intra-uterine pressure sustained above 80 mm.Hg for 1 minute in 4½ minutes. The uterus relaxed incompletely between contractions. Foetal distress developed in a period of 20 minutes and the baby was rescued by anaesthesia and forceps delivery. The peak intra-uterine pressure was 160 mm.Hg.

Fig. 14.
Intra uterine pressure readings in second stage of labour to demonstrate risk to the foetus.
(Williams, 1952)

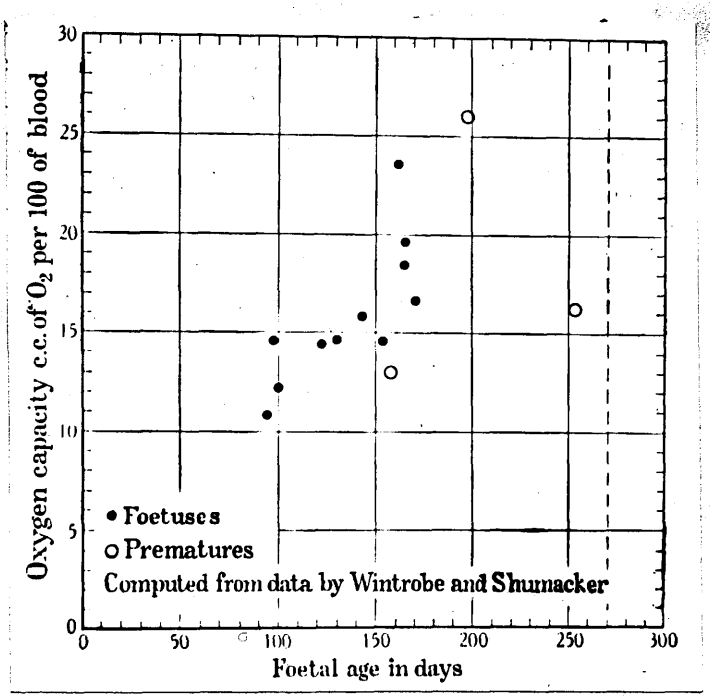



Fig. 15.
Oxygen capacity of the human foetus at successive foetal ages. (Wintrobe and Shumacker, 1936)

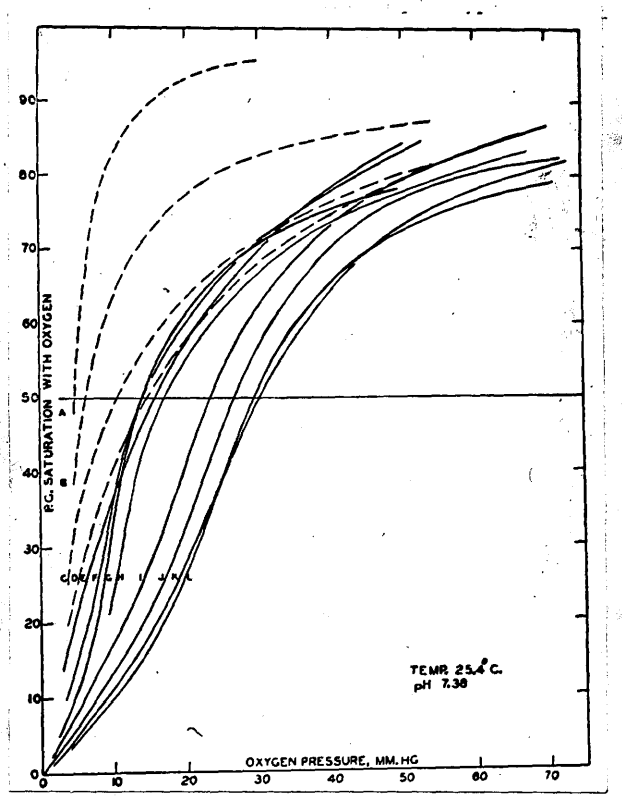



Fig. 16.
Dissociation curves of the haemoglobin of tadpole and bull frog at various stages in life history to show the change in shape and position of the curves. The broken line is the tadpole and age increases from A to L. (McCutcheon, 1936).

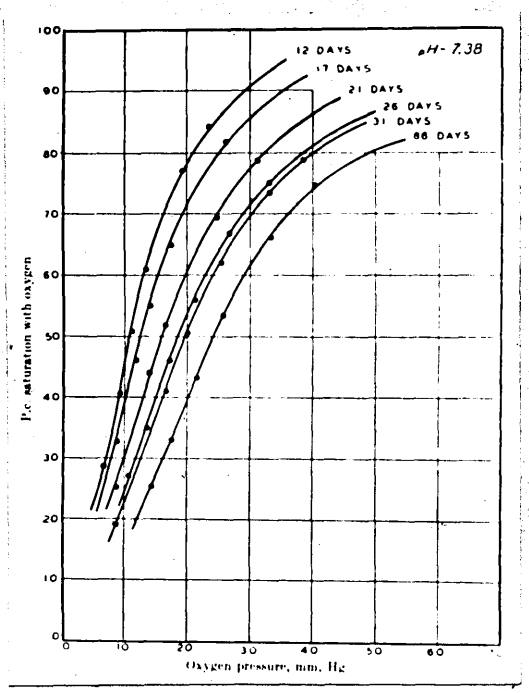



Fig. 17.
Dissociation curves of haemoglobin of chick during development. Age as from onset of incubation.
(Hall, 1935)

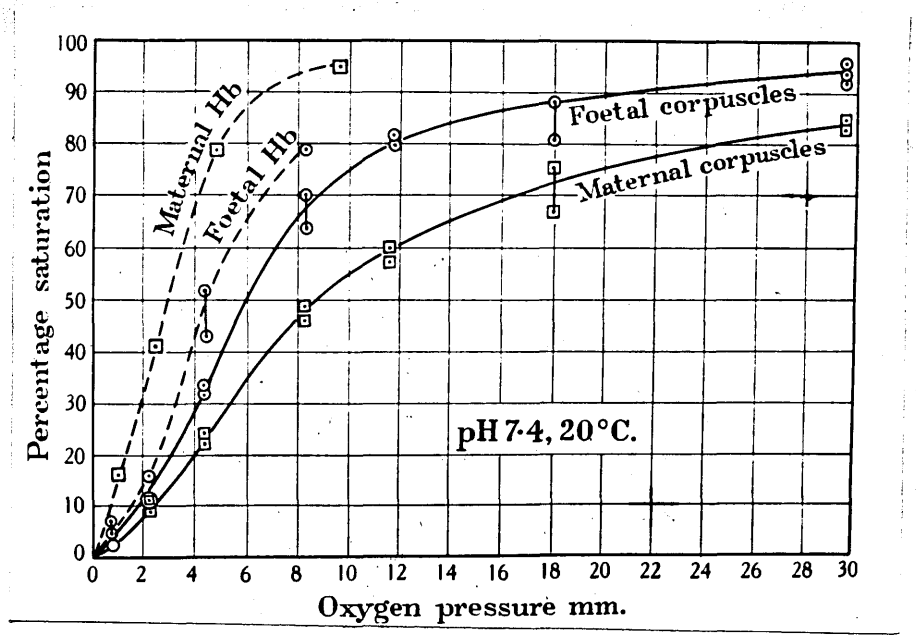



Fig. 18.
Comparison between dissociation curves of haemoglobin and corpuscles respectively in the human adult and foetus. (Hill, 1935)

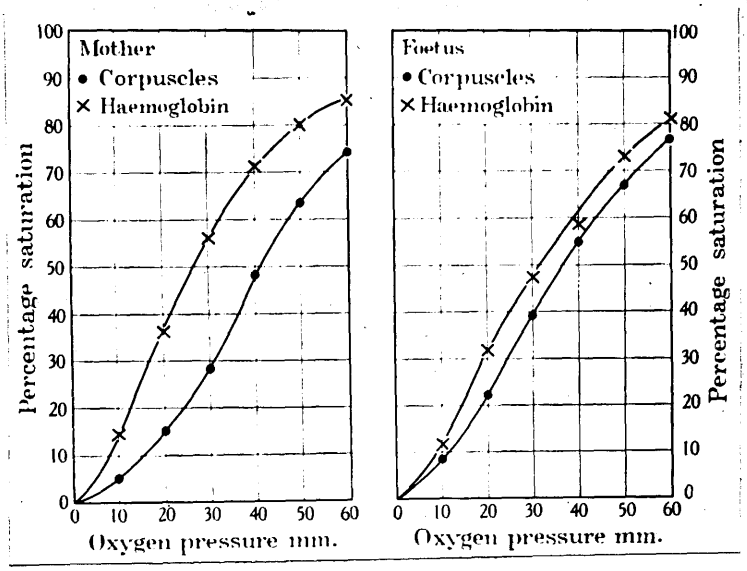



Fig. 19.
Dissociation curves of human corpuscles and haemoglobin in strong solution. Demonstrates the marked effect of maternal corpuscular membrane of adult cells and the normal effect of the membrane of foetal blood cells. (McCarthy, 1943)

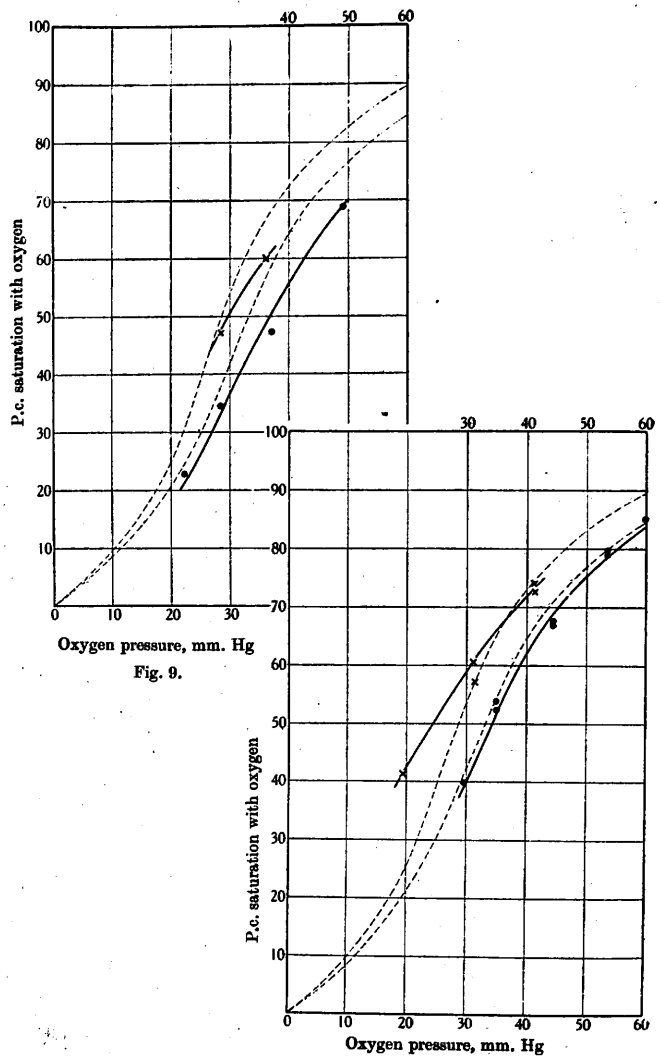



Fig. 20. Dissociation curve of the blood of the goat foetus and of its mother. (Barcroft et al, 1935)

(9) 79 days
(10) 106 days of foetal life.

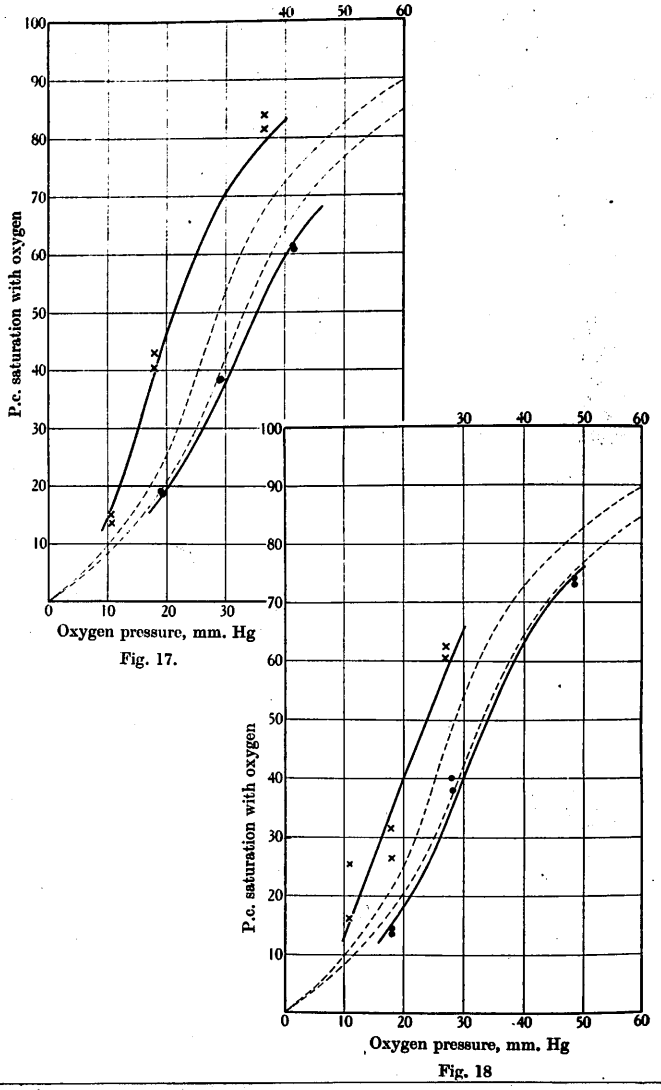



Fig. 20. Dissociation curve of the blood of the goat foetus and of its mother. (Barcroft et al, 1935)

(17) 136 days
(18) 144 days of foetal life. (Term = 142 ± 2 days)

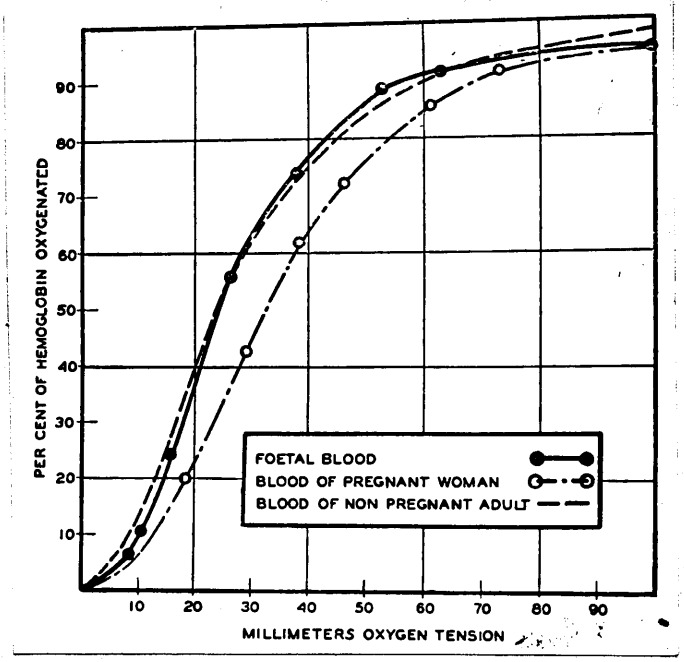



Fig. 21.
Dissociation curve of human maternal and foetal blood.
(Eastman, et al, 1933)

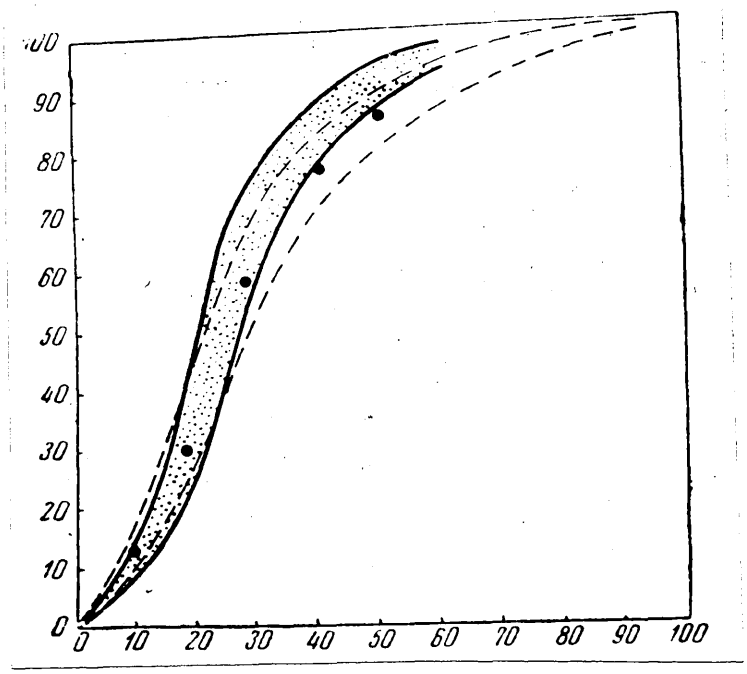



Fig. 22.
Dissociation curves of the blood of the human foetus at early and late periods of gestation. (Sachs and Likhnizkaya, 1938) Stippled area shows - curves up to the 35th week.

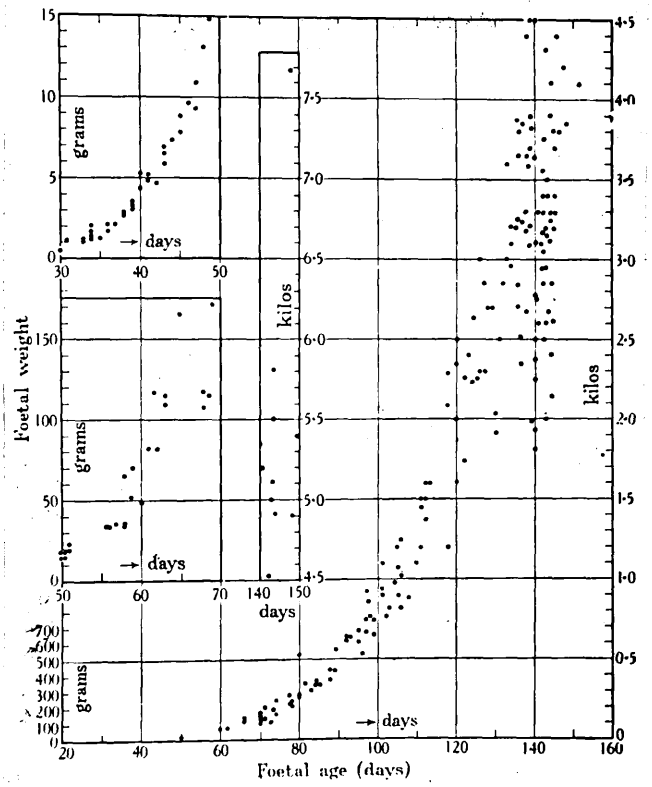



Fig. 23.
The relation of foetal age to weight in the sheep.
(Barcroft, 1945)

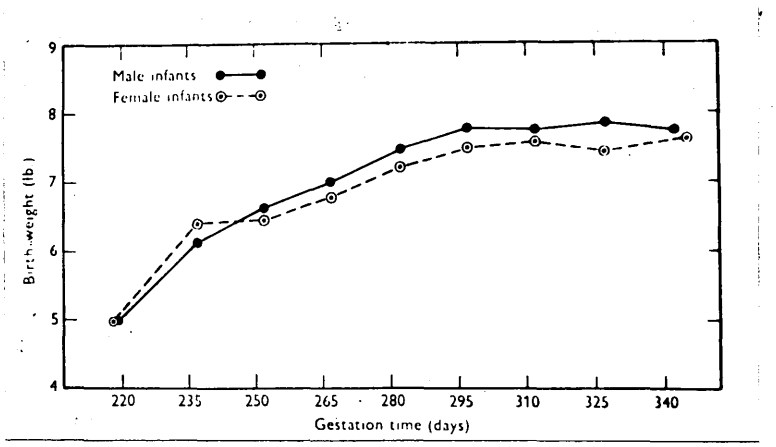



Fig. 24.
The relation of foetal age to weight in the human (mean values). (Karn and Penrose, 1951)

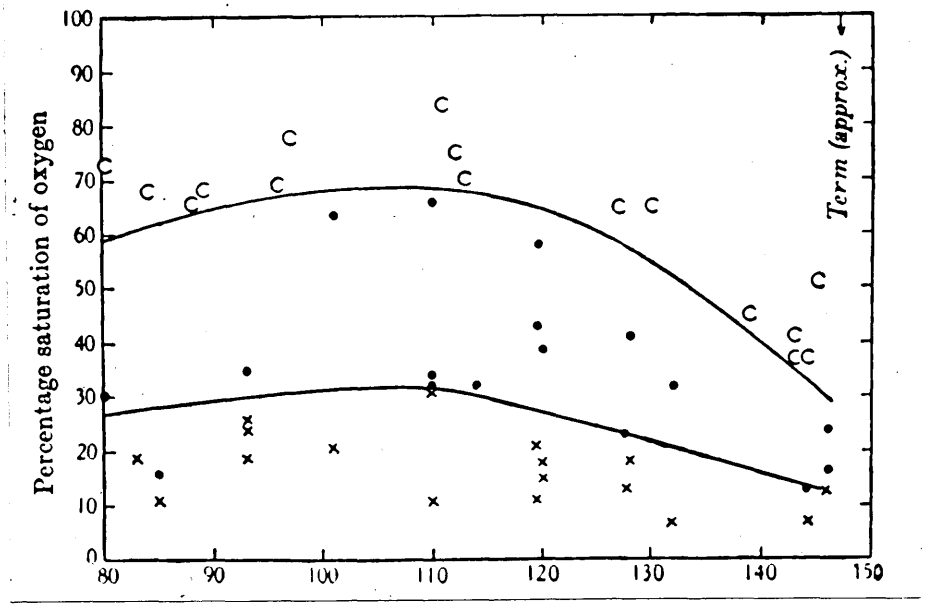
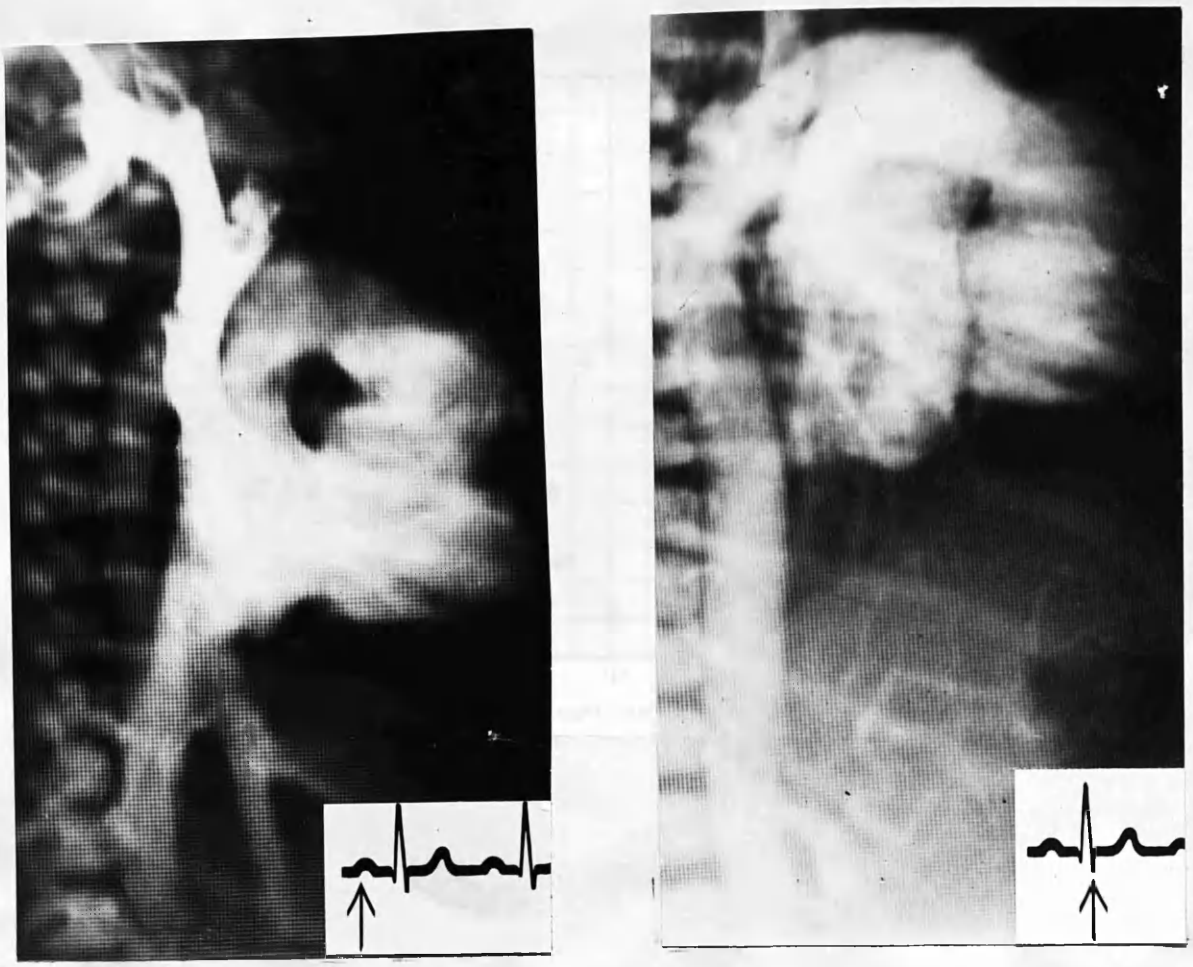



Fig. 25.
Percentage saturation with oxygen of the blood of the foetal sheep in c carotid artery, o venous sinuses of brain and x venous sinuses when respiratory movement had appeared after puncturing the umbilical cord.
(Barcroft et al, 1938).

Fig. 26.
Injection of contrast medium through the umbilical vein of the human foetus. (Lind, 1953)

(a) Right anterior oblique position. Contrast filling vascular network of liver, ductus venosus, hepatic veins and inferior vena cava. Contrast just enters auricle.

Fig. 27.
Injection of contrast medium through the umbilical vein of the human foetus. (Lind, 1953).
The hepatic veins and the inferior vena cava visualised. Contrast medium is flowing into the auricles, the stream being divided by the crista dividiens.



(a) (b)

Fig. 28. A full term newborn with intense cyanosis. Angio-:cardiography (arm vein) 4 hours after birth. (Lind, 1953)
(a) Superior vena cava, right atrium, right ventricle and aorta are visualised.
(b) Aorta and pulmonary arteries filled. The fact that dye is seen in aorta before it is seen in the pulmonary arteries is explained by passage of most of the medium through the patent ductus arteriosus. Seven days later angiocardiography normal.

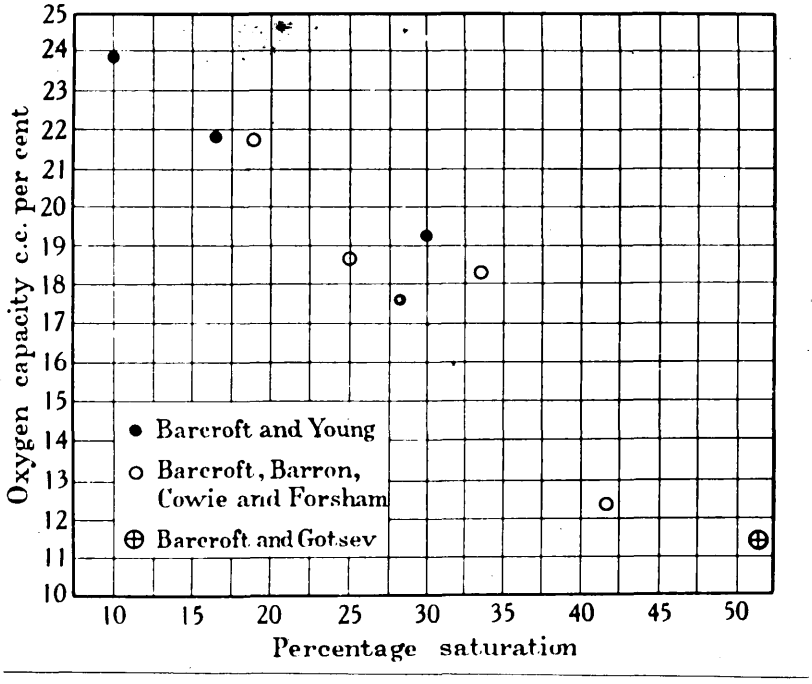



Fig. 29.
Correlation between oxygen capacity and percentage saturation of blood in the umbilical artery (quoted by Barcroft, 1946)

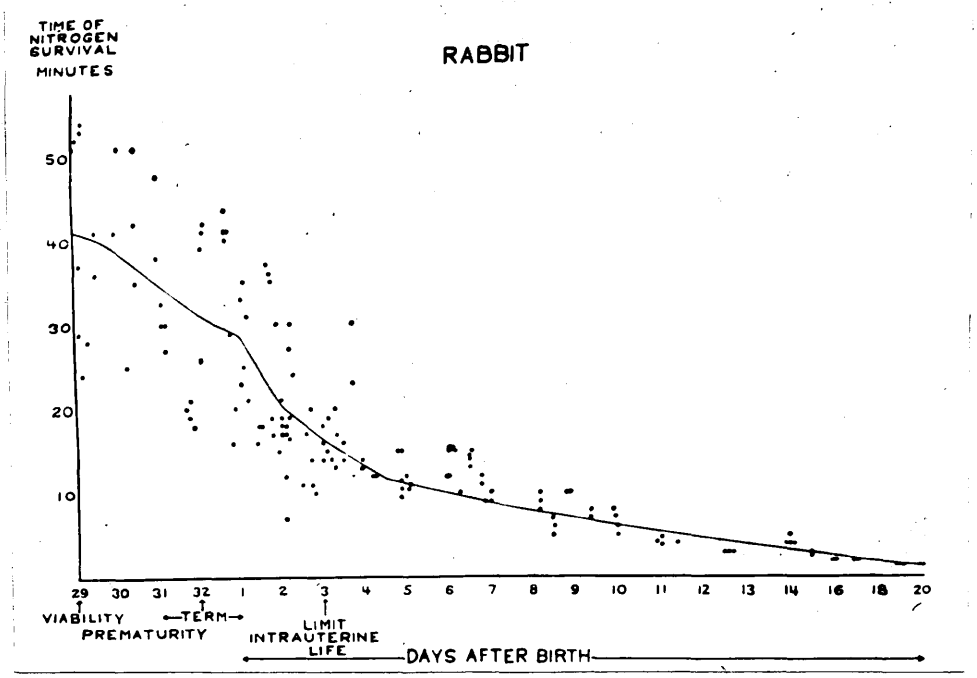



Fig. 30.
Decline in resistance to anoxia with advancing age, foetal and newborn rabbits. (Glass et al, 1944)

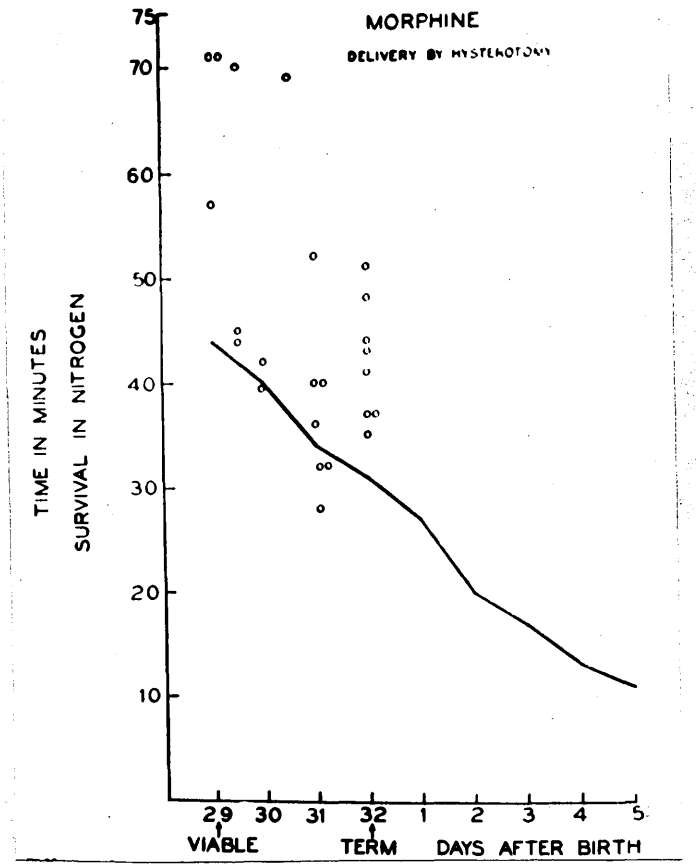



Fig. 31.
Increase in resistance to anoxia in the newborn rabbit after a moderately heavy dose of morphia to the mother.
(The heavy line shows the average resistance of non-narcotized foetuses). (Snyder and Geiling, 1943)

Fig. 32. Extraction of blood sample from umbilical vein. This is a particularly small segment of cord and only 2 ml. of blood could be obtained.

Fig. 33. Anaerobic sealing of syringe. Glass rod pushed home into rubber collar - blood being forced past the rod as it is pushed home.

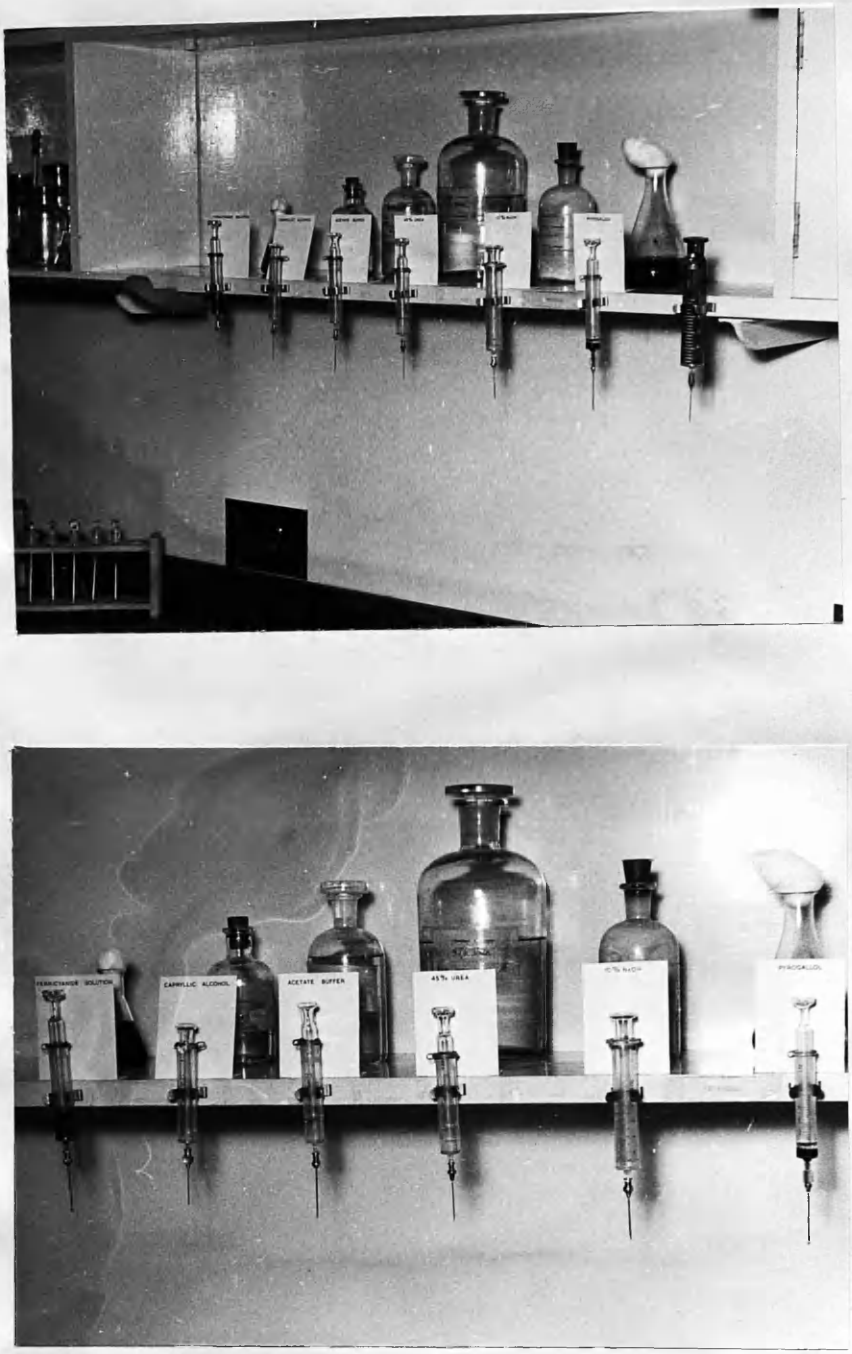



Fig. 34. The reagents. Using solutions in a syringe bank. Each syringe barrel is liberally greased with vaseline to aid movement.

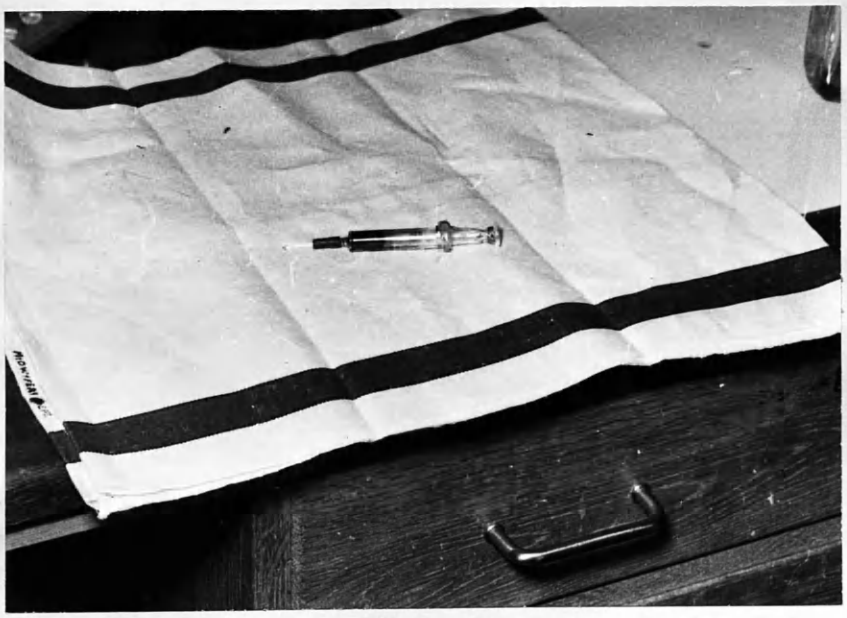


Fig. 35. Syringe with rubber cap and glass seal ready for estimation.

Fig. 36. Filling pipette from blood syringe. Plunger is being pushed in gently by little finger of right hand.

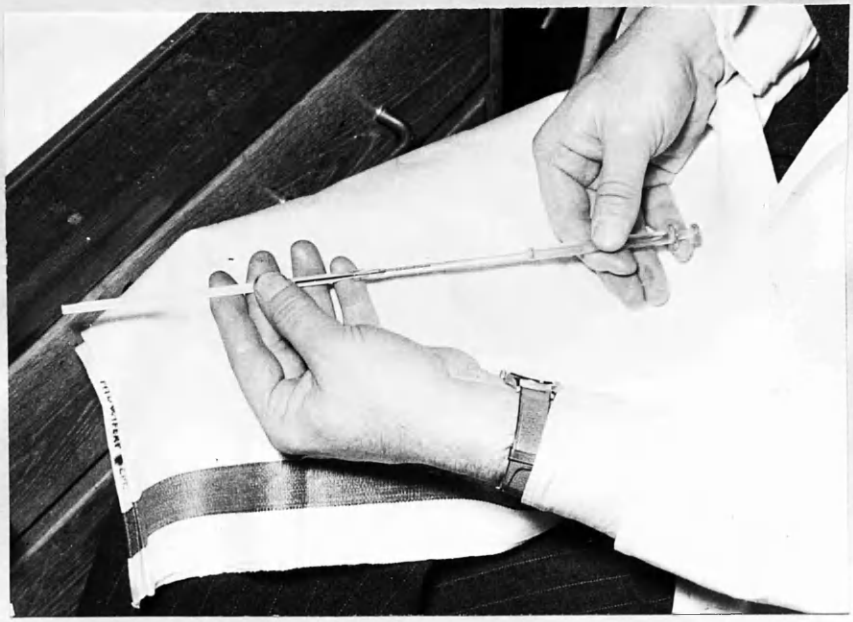


Fig. 37. Filling of Roughton and Scholander syringe from blood pipette. Note method of holding syringe and pipette. Plunger is being withdrawn by little finger of right hand, the syringe being slightly below the level of the pipette to utilise gravity.

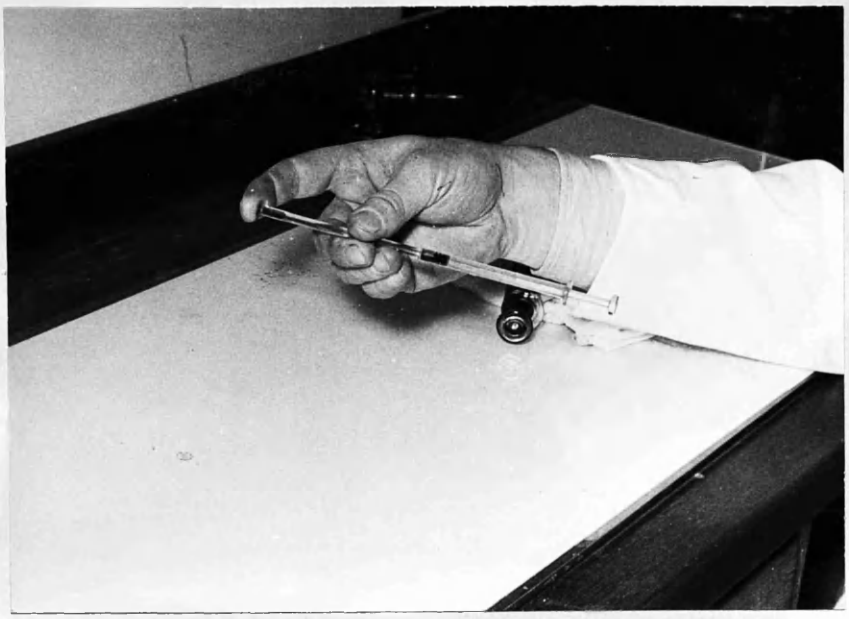


Fig. 38. Gas extraction by shaking. Clip is off. Syringe is shaken in position as shown but in vertical direction.

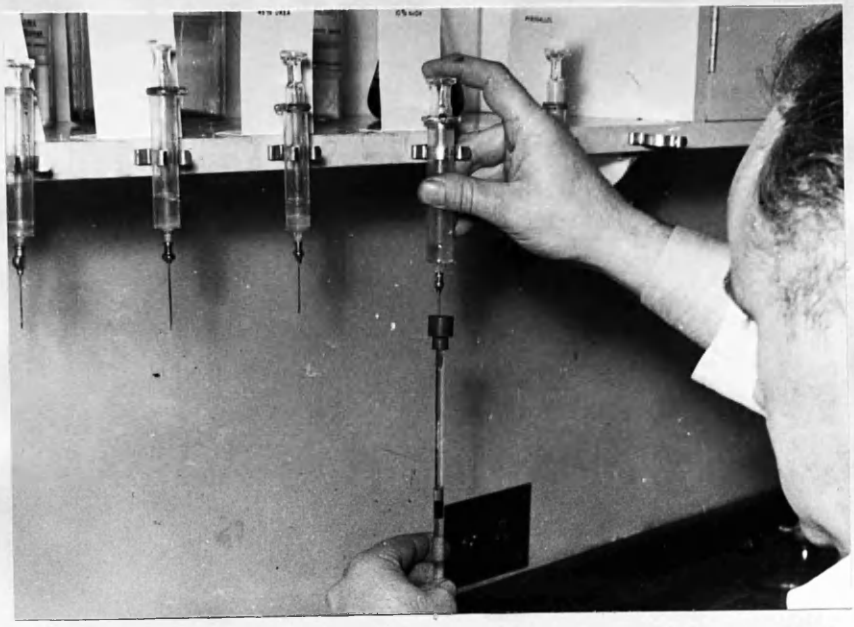


Fig. 39. Filling the cup with 10 per cent. Na O H before absorption of $CO_2$ to illustrate use of the syringe bank.

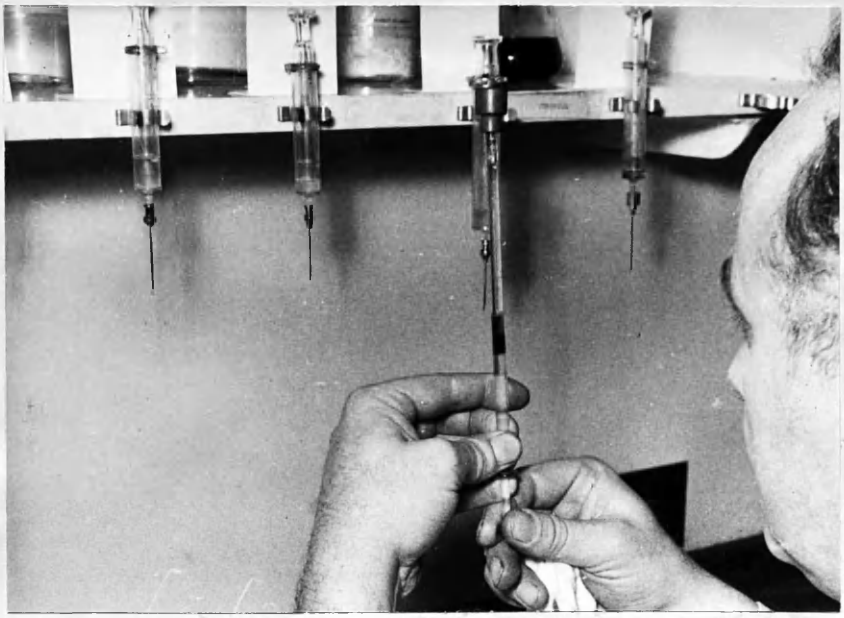


Fig. 40. Adjustment of gas bubble in capillary.
Note little finger of left hand as a brake on plunger and movement of plunger by rotatory movement of fingers of right hand.

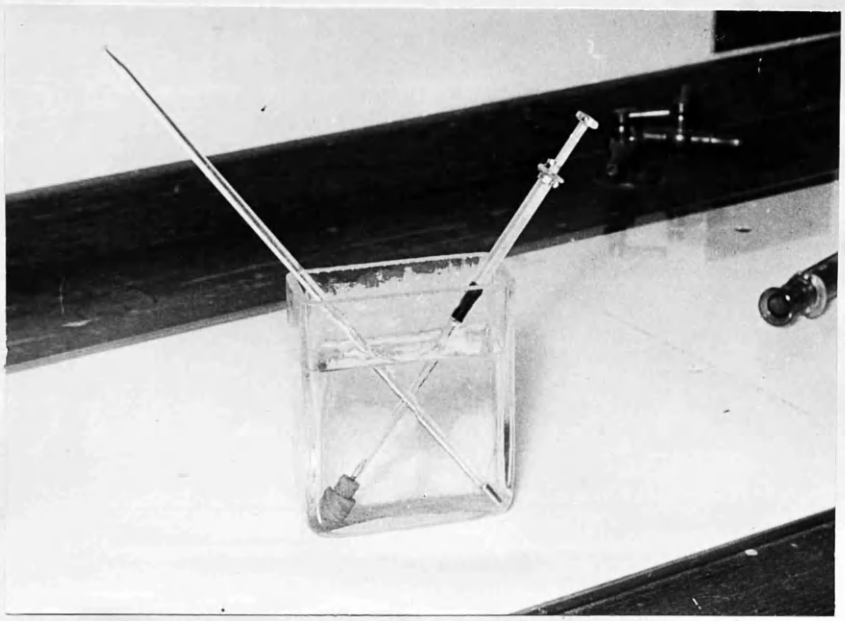


Fig. 41. Equilibration of gas bubble at a definite temperature after absorption of $CO_2$. Clip is on.

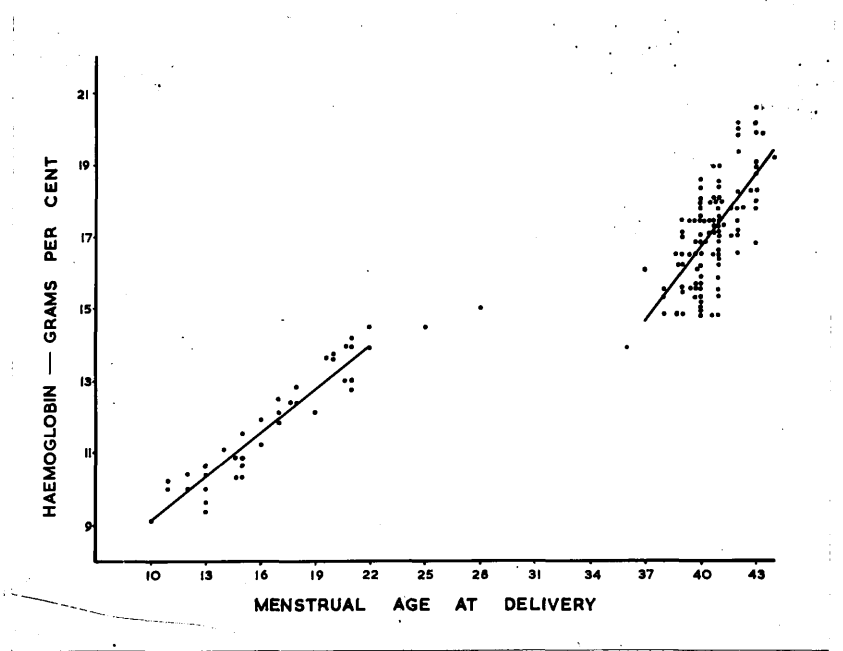



Fig. 42. Haemoglobin levels in cord blood of human foetus in normal pregnancy.

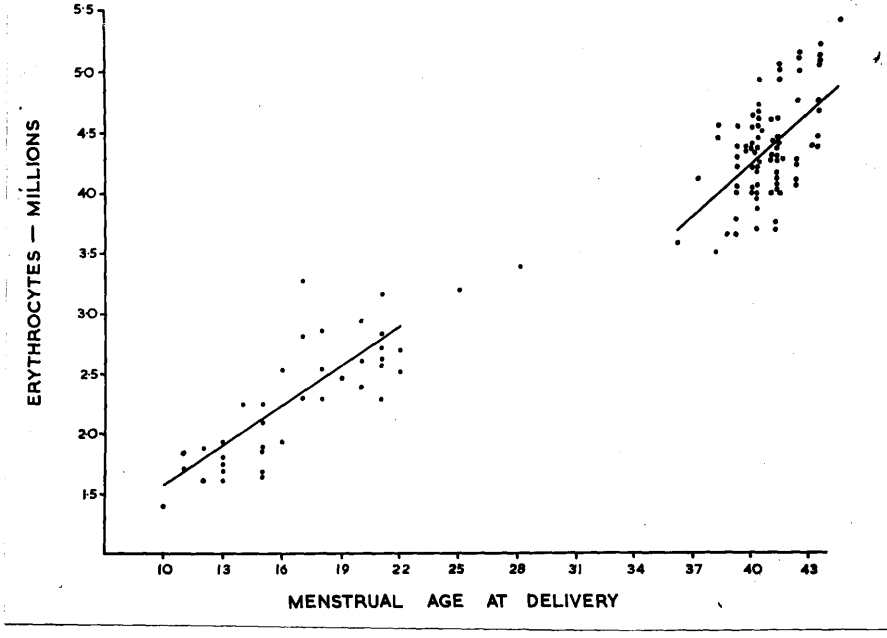



Fig. 43.
Red-cell count in cord blood of human foetus in normal pregnancy.

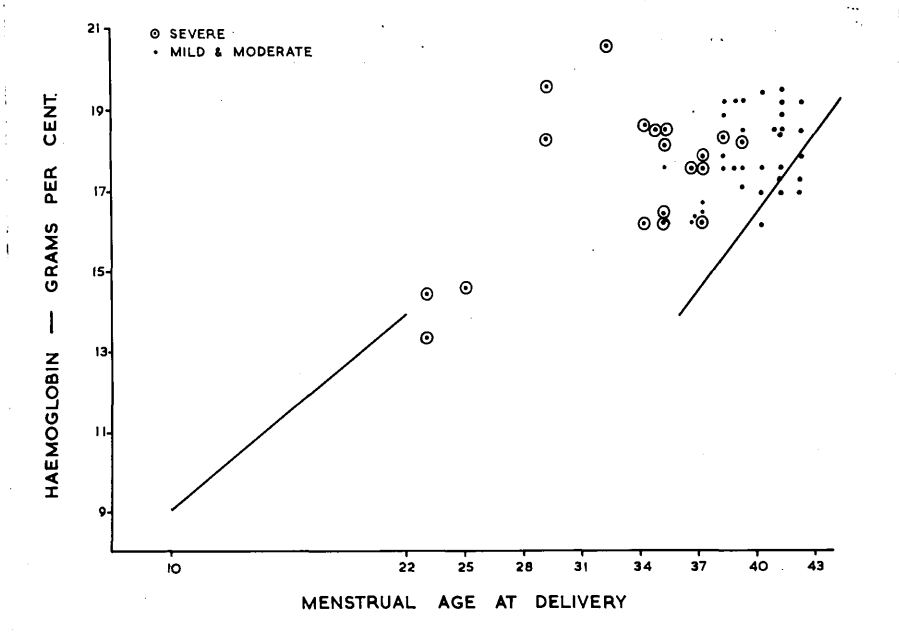



Fig. 44. Haemoglobin levels in cord blood in pre-eclampsia.

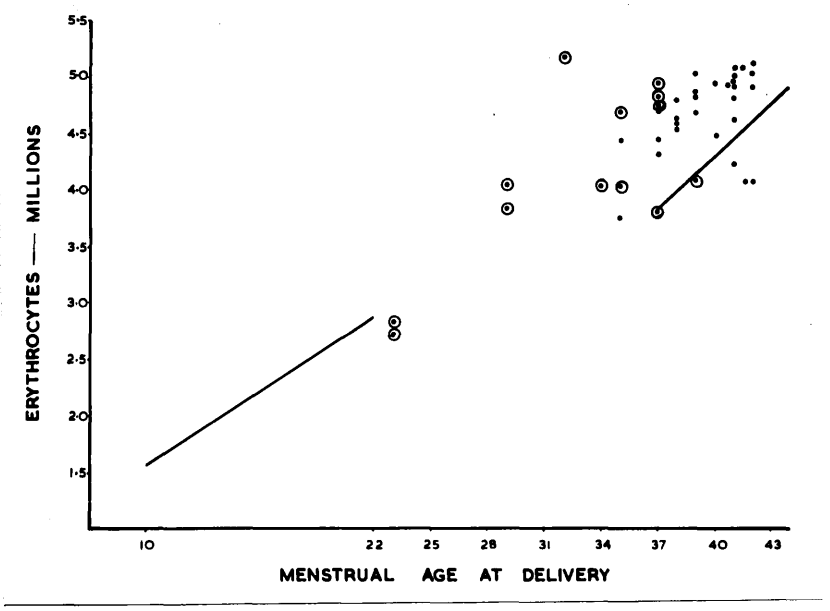



Fig. 45. Red-cell count in cord blood in pre-eclampsia.
(⊙ Severe • Mild and moderate pre-eclampsia)

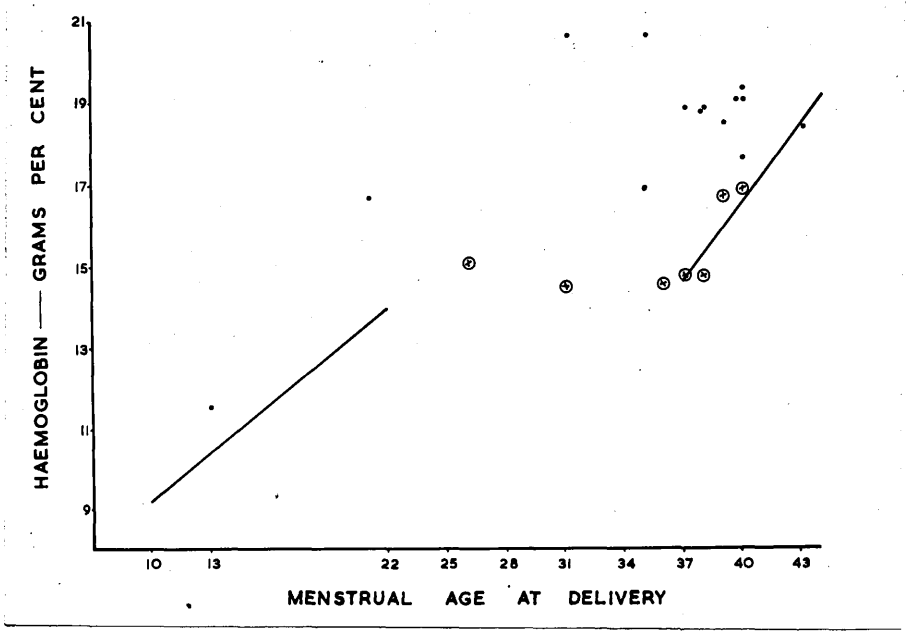



Fig. 46. Haemoglobin levels in cord blood in cases in which abortion had threatened earlier in the pregnancy ( • ) and in proved placenta praevia. ( ⊗ )

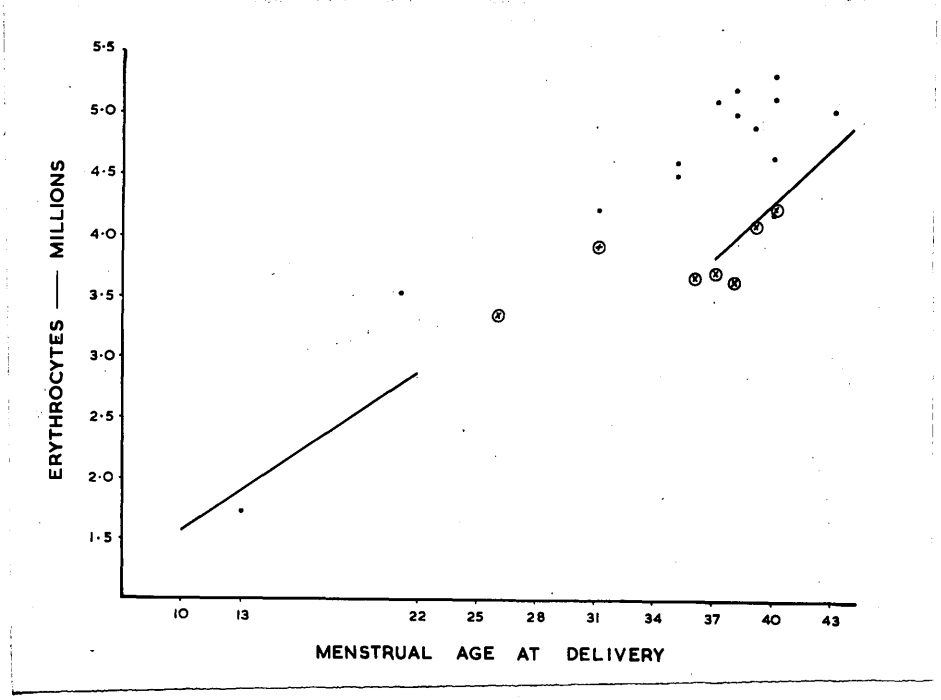



Fig. 47. Red-cell count in cord blood in cases in which abortion had threatened earlier in the pregnancy (•) and in proved placenta praevia.( ⊗)

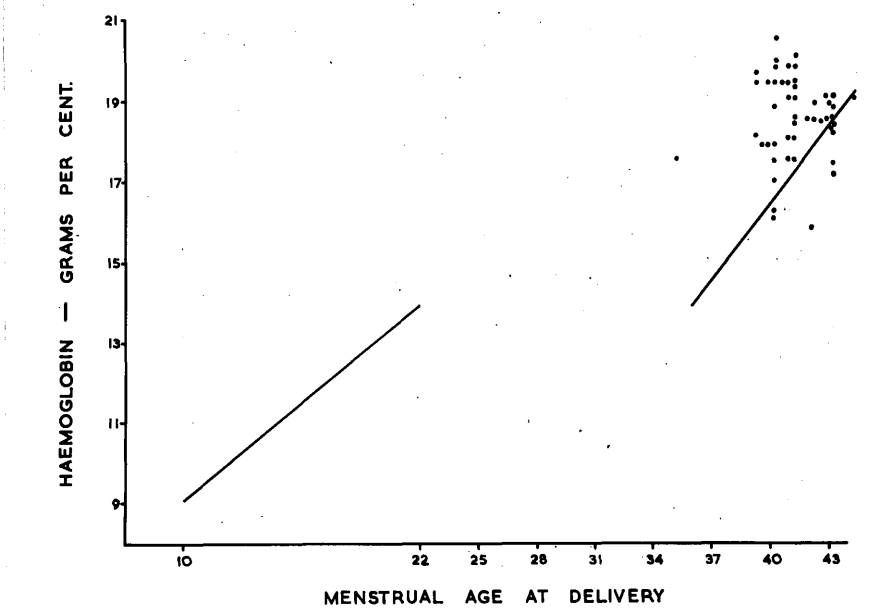



Fig. 48. Haemoglobin levels in cord blood in cases where foetus showed clinical evidence of distress.

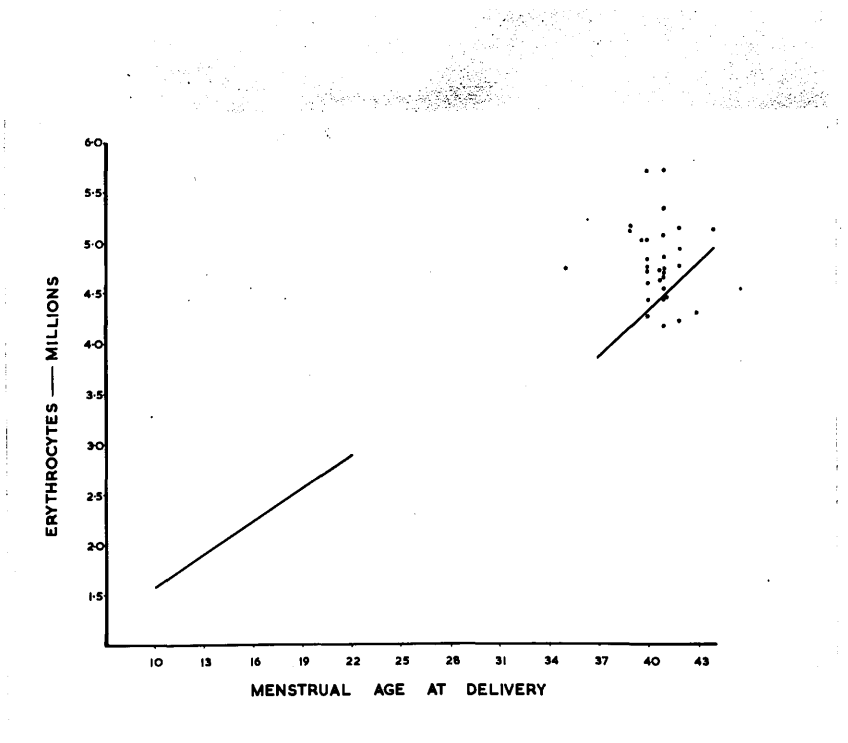



Fig. 49. Red-cell count in cord blood in cases where foetus showed clinical evidence of distress.

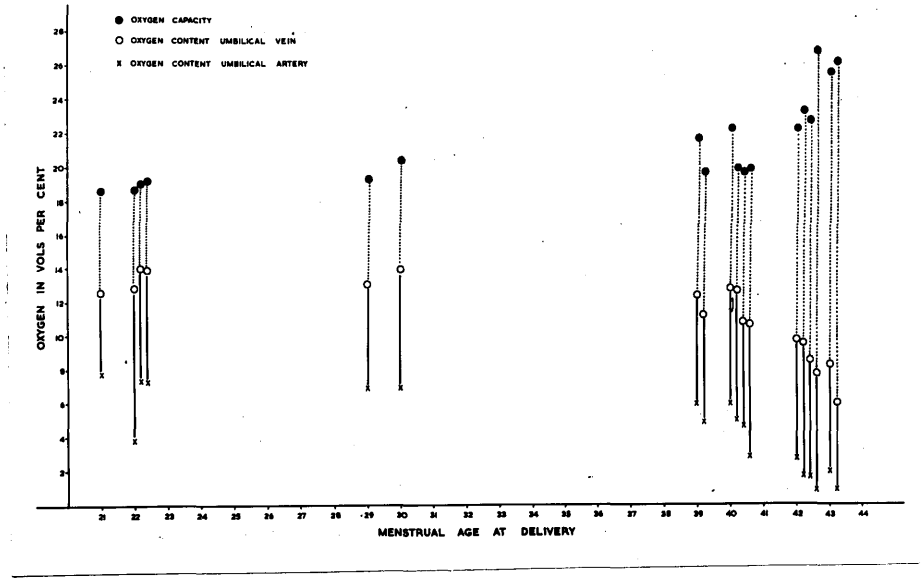



Fig. 50. Oxygen capacity and content of cord blood of human foetus in normal pregnancy.

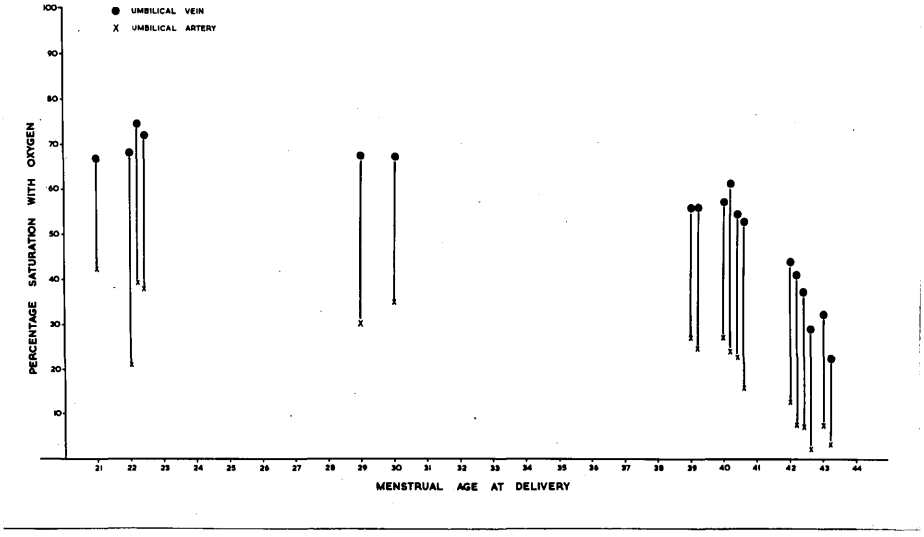



Fig. 51. Percentage saturation with oxygen of cord blood of human foetus in normal pregnancy.

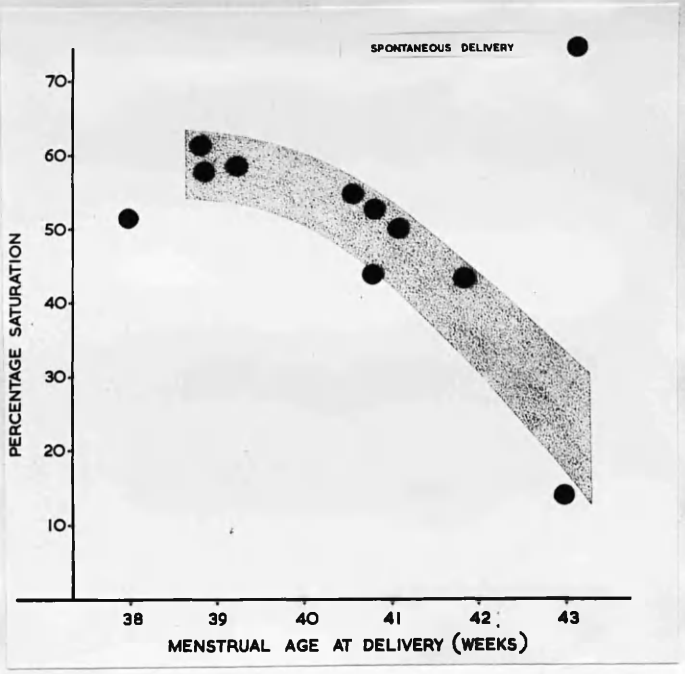



Fig. 52. Percent. saturation with oxygen of blood in the umbilical vein at spontaneous delivery (without evidence of meconium staining) plotted against range of readings found before the onset of labour. (Fig. 51)

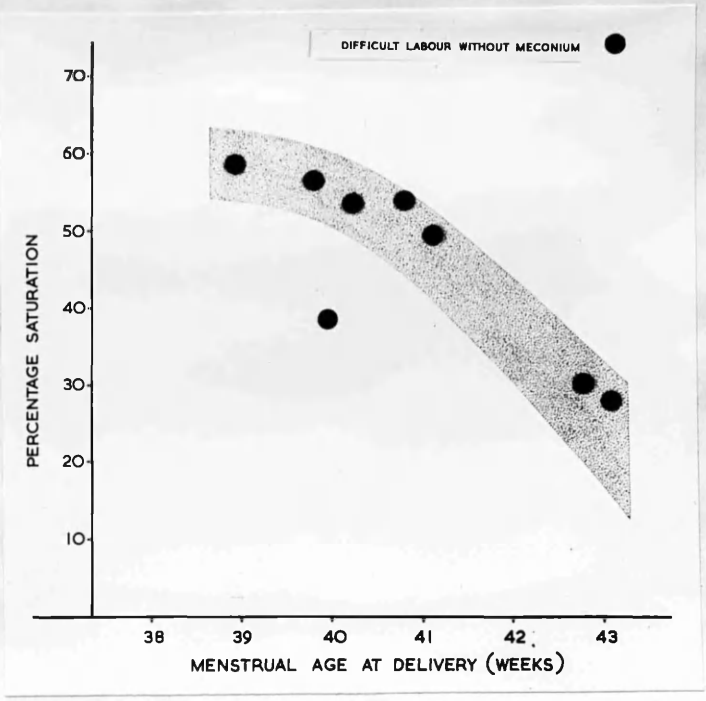



Fig. 53. Percent. saturation with oxygen of blood in the umbilical vein after prolonged or difficult labour (without evidence of meconium staining) plotted against range of readings found before the onset of labour. (Fig. 51).

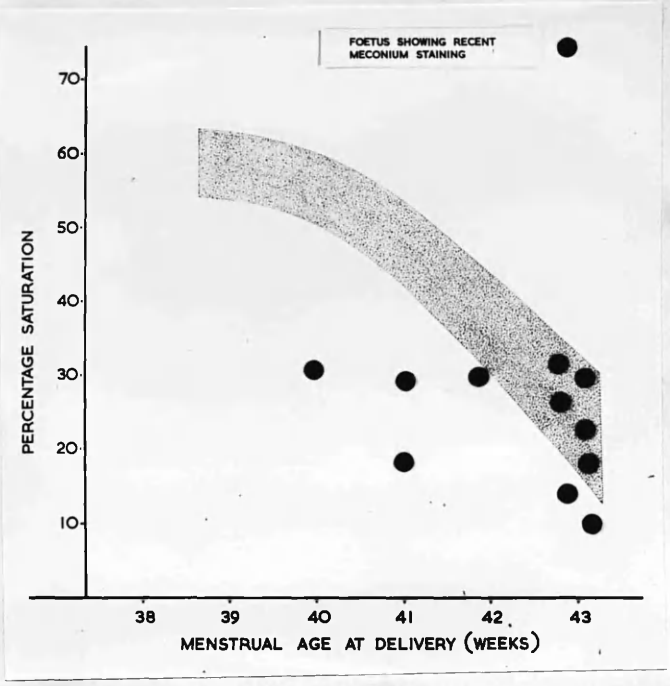



Fig. 54. Percent. saturation with oxygen of blood in the umbilical vein where the foetus has recently passed meconium, plotted against range of readings found before the onset of labour. (Fig. 51)

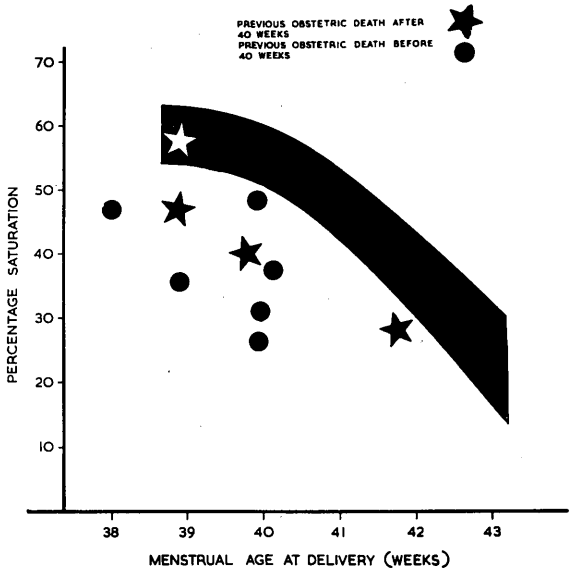



Fig. 55. Percent. saturation of blood in umbilical vein at Caesarean Section under spinal anaesthesia where previous pregnancy has been lost by stillbirth or early neonatal death, plotted against range of readings found before the onset of labour (Fig. 51).

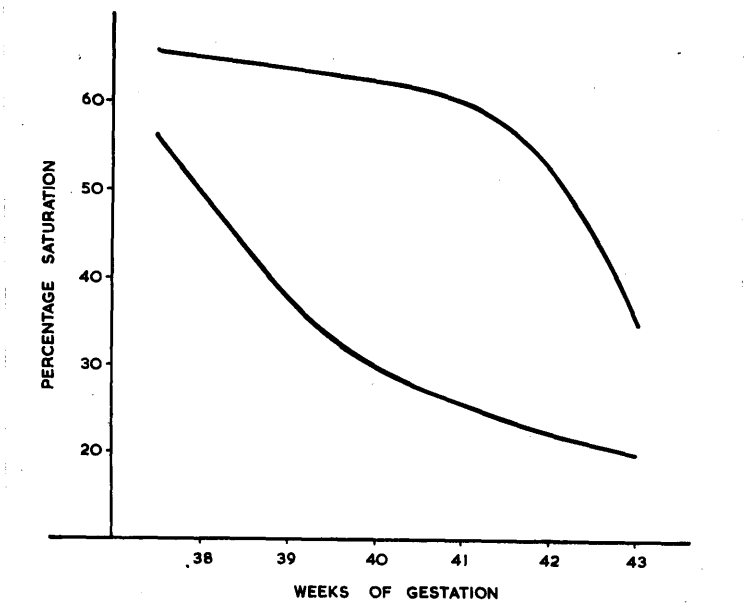



Fig. 56. Percent. saturation with oxygen in umbilical vein - the range of values likely to be found in clinically normal pregnancy at Caesarean Section before the onset of labour.

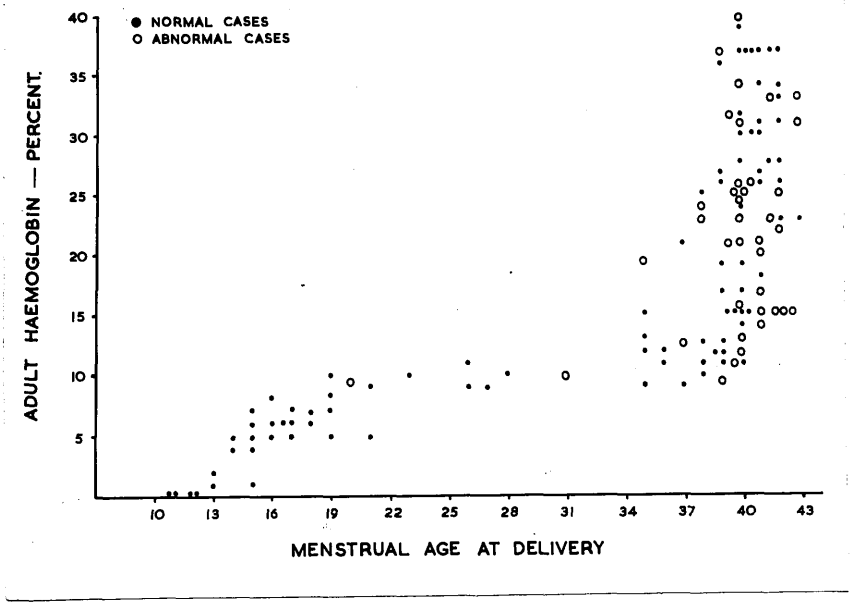



Fig. 57. The percentage of adult type haemoglobin in the blood of the human foetus at various stages of gestation.

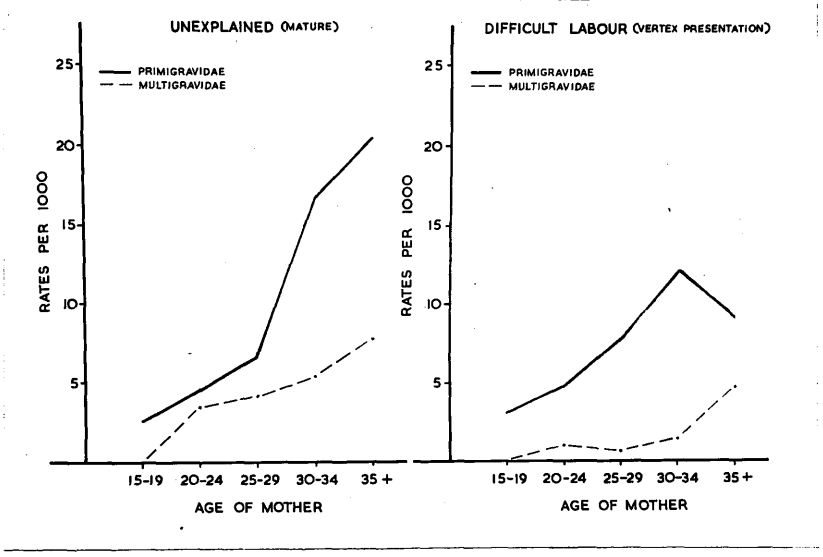



Fig. 58. The obstetric death rate in Mature Unexplained and Difficult Labour clinical groups by parity and maternal age.

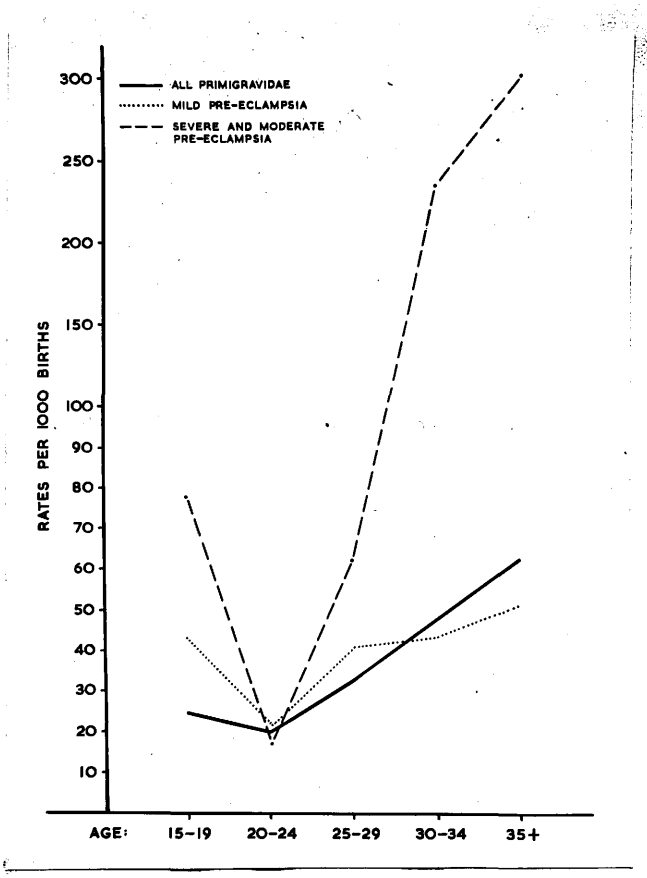



Fig. 59. The stillbirth rate per 1000 cases of pre-eclampsia in primigravidae depending on the severity of the disease compared with the stillbirth rate for all deliveries.

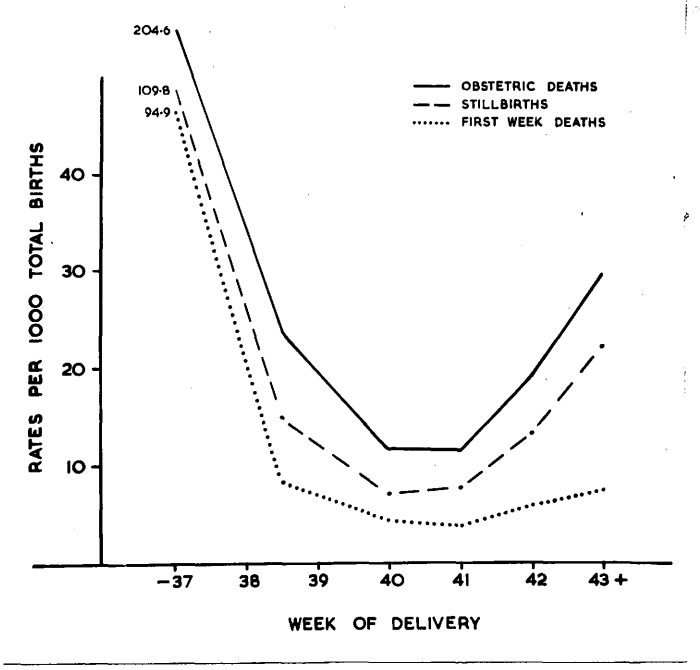



Fig.60. Obstetric death, stillbirth and first week neonatal death rates per 1000 total births all parities.

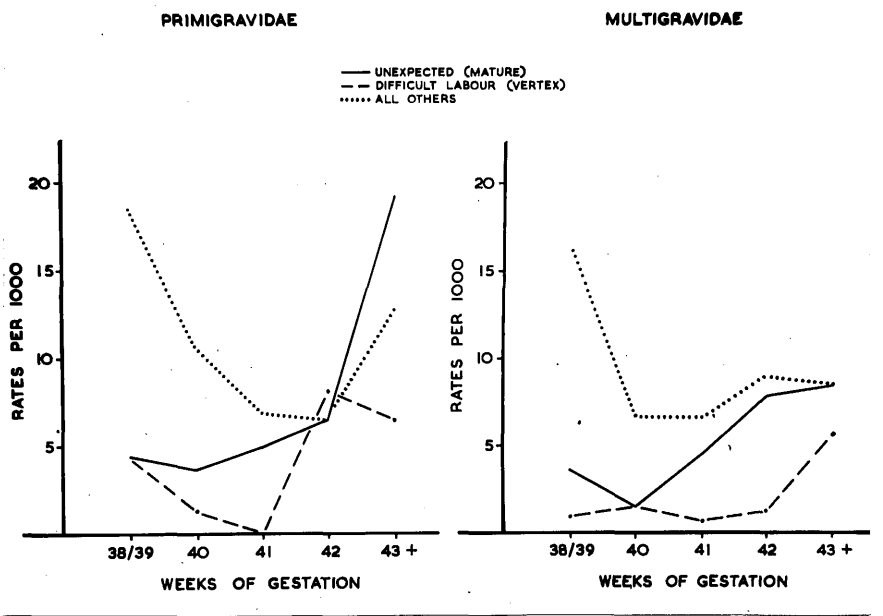



Fig.61. Obstetric deaths in late pregnancy by clinical cause of death.

For "unexpected (mature)" read "unexplained (mature)".

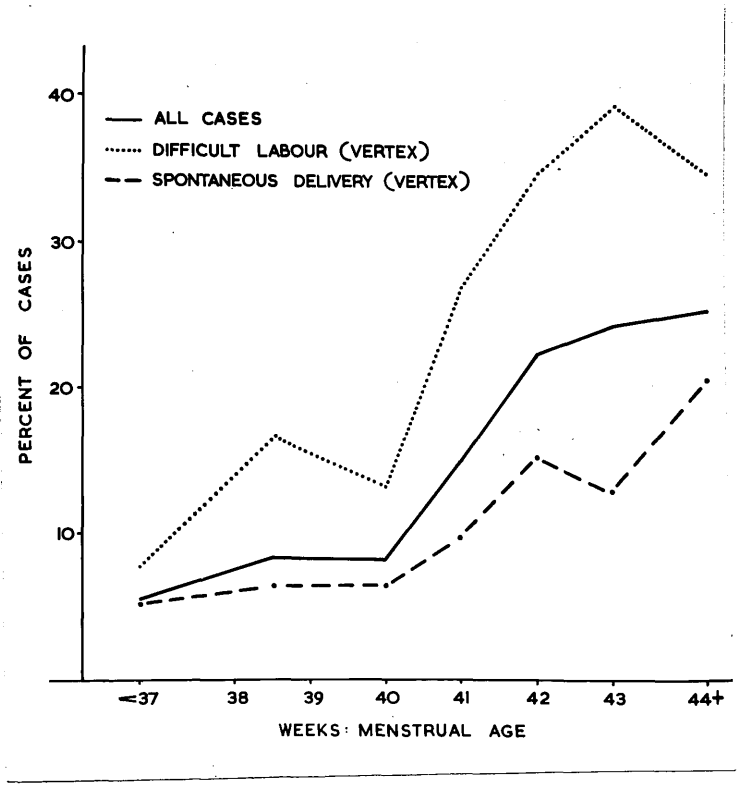



Fig. 62. Foetal distress in primigravidae.
Incidence by type of labour by week in which delivery took place.

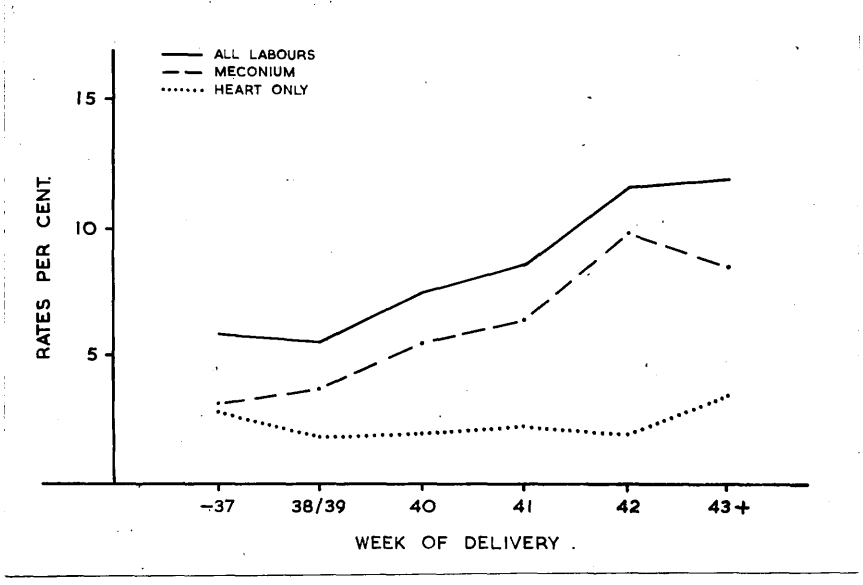



Fig. 63. Foetal distress in multigravidae. Incidence in all labours and by type of distress manifest.

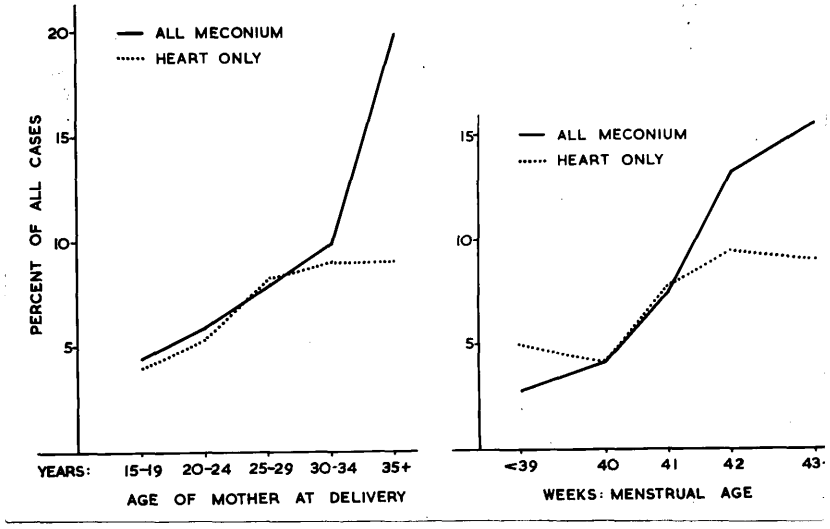



Fig. 64. Foetal distress in primigravidae.
Type of distress manifest in relation to maternal age and week in which delivery took place.

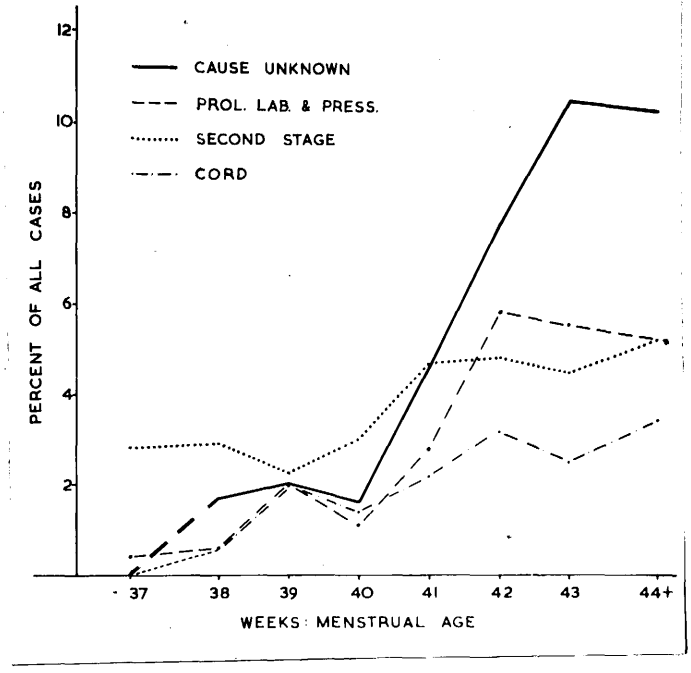



Fig. 65. Foetal distress in primigravidae. Clinical cause of distress by week in which delivery took place.

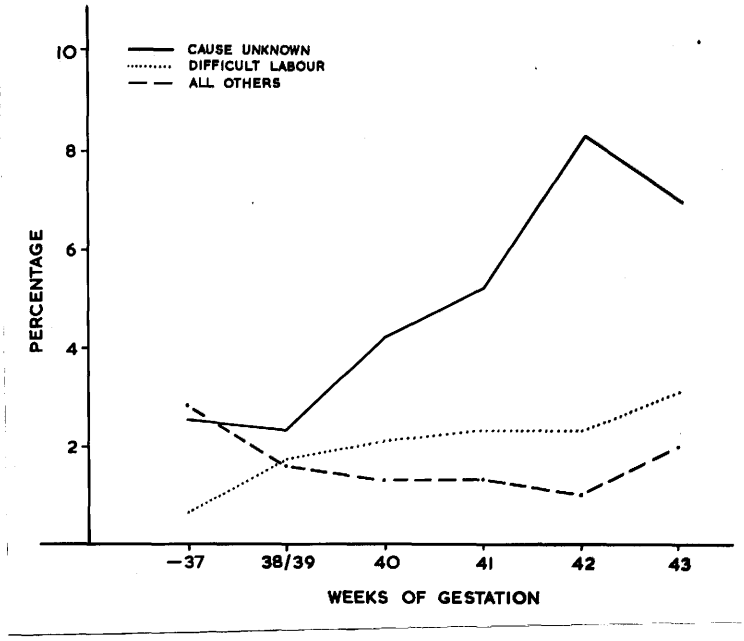



Fig. 66. Foetal distress in multigravidae. Clinical cause of distress by week in which delivery took place.

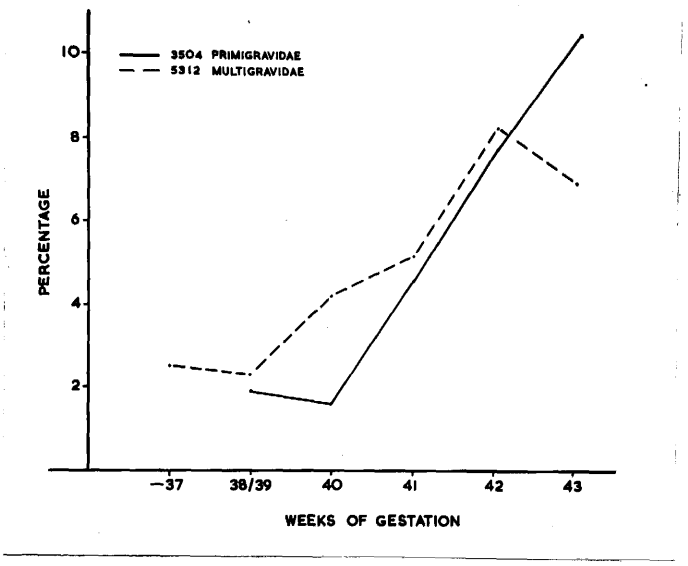



Fig. 67. Foetal Distress - unknown cause - the relation between incidence in primigravidae and multigravidae.

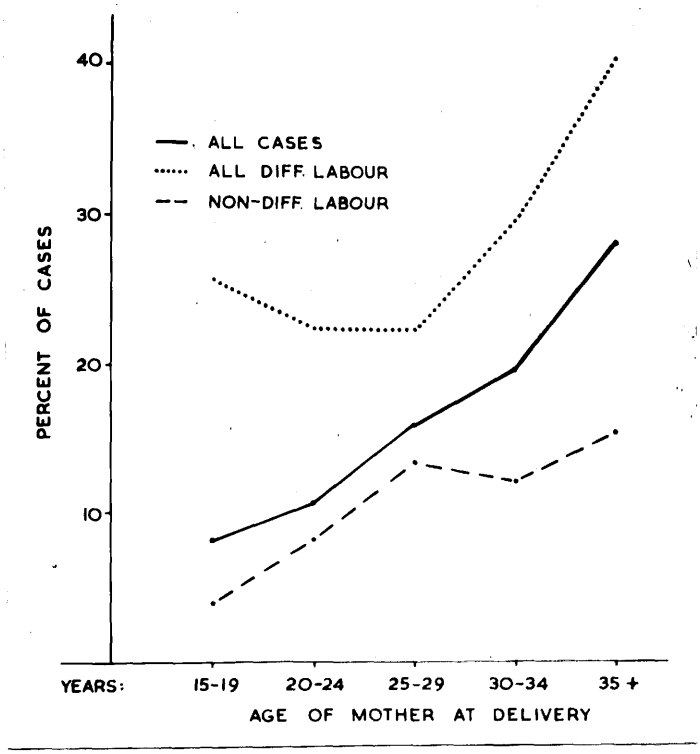



Fig. 68. Foetal distress in primigravidae. Incidence by type of labour in relation to the age of the mother.

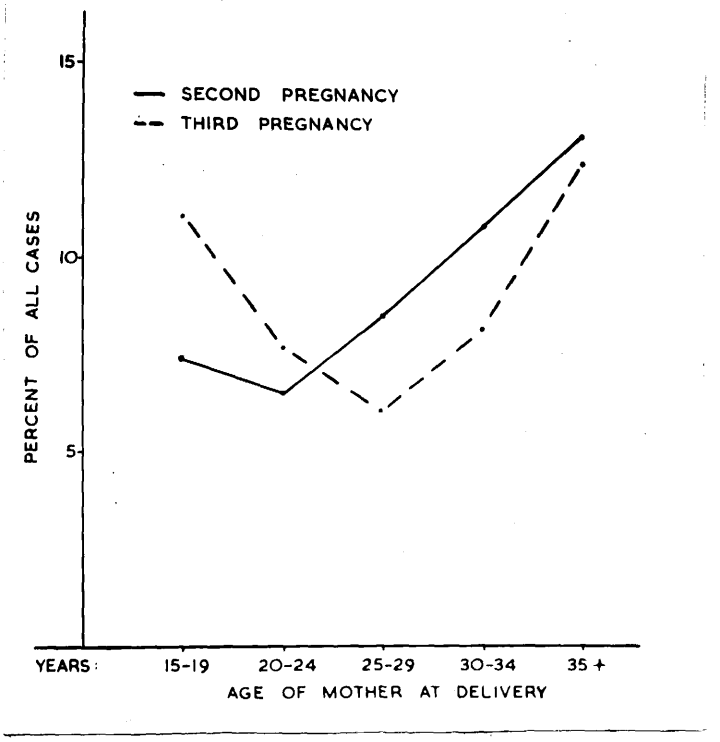



Fig. 69. Foetal distress in multigravidae.
Incidence in relation to the age of the mother.

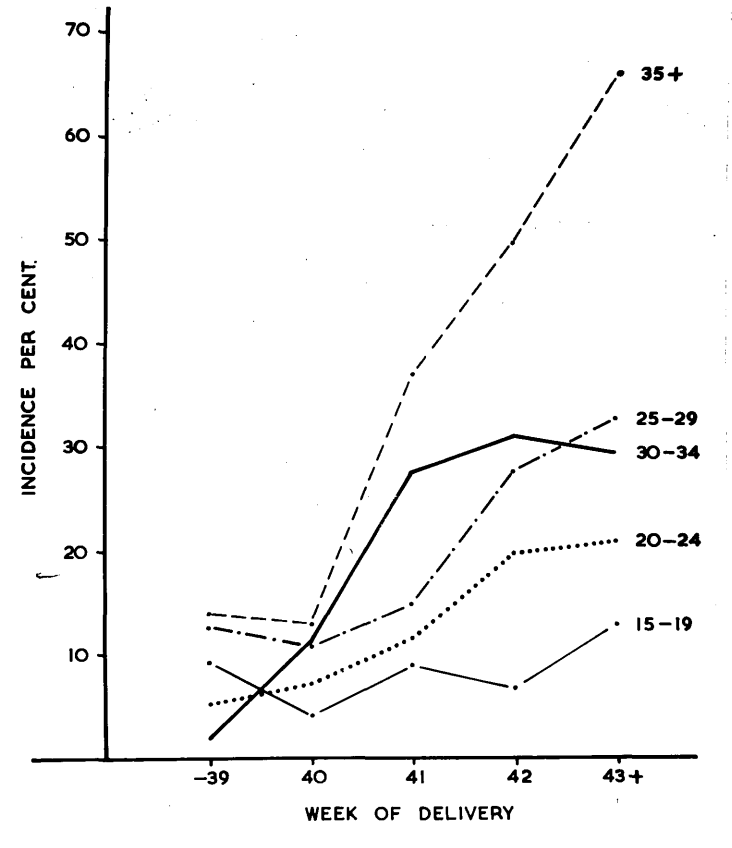



Fig. 70. Foetal distress in primigravidae. Incidence in various maternal age groups by week in which delivery took place.

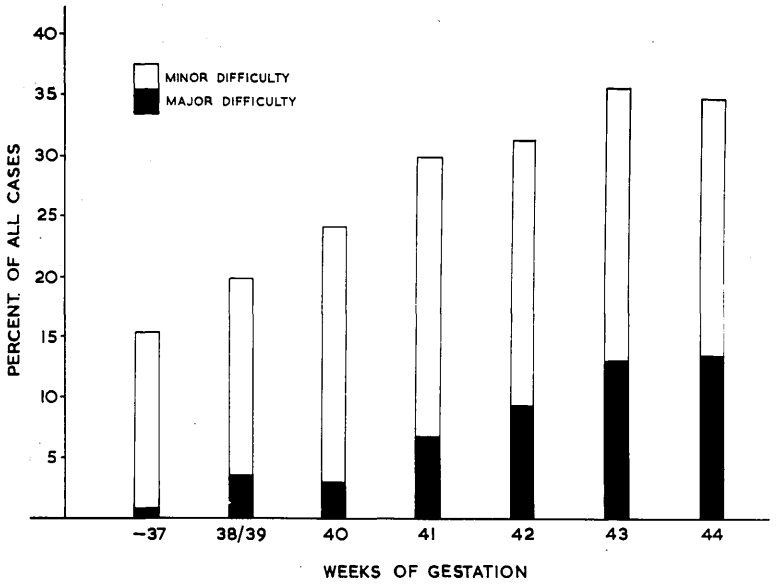



Fig. 71.
Incidence of difficult labour in primigravidae (vertex presentation only).

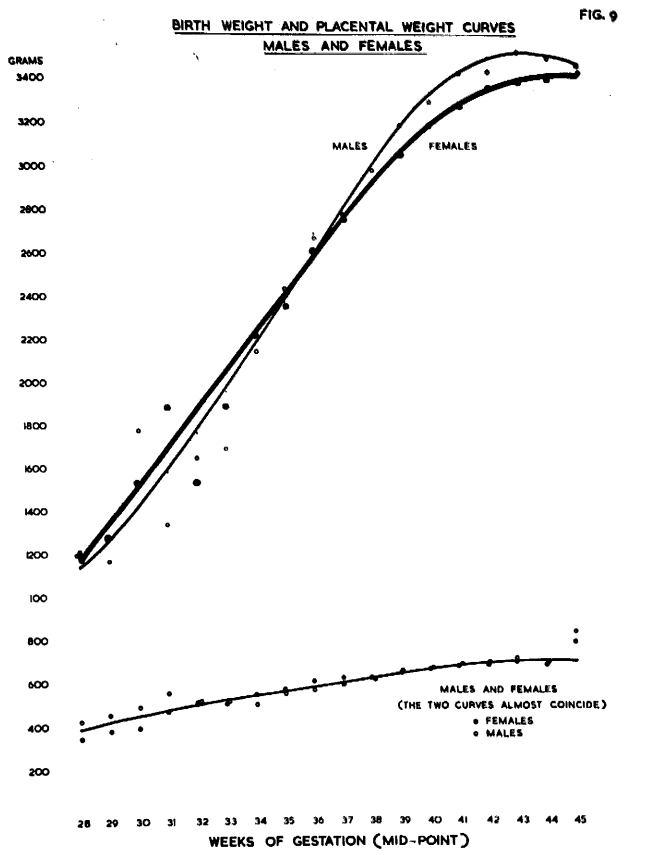



Fig. 72.
Birth weight and placental weight curves (mean readings only).

(2) TABLES.

## TABLE I.

## OXYGEN IN THE UMBILICAL VESSELS OF THE HUMAN FOETUS BEFORE THE ONSET OF LABOUR.

| Author. | Oxygen Content Vols. %. | | Oxygen Saturation. % | | Remarks. |
|---|---|---|---|---|---|
| | Vein. | Artery. | Vein. | Artery. | |
| Haselhorst and Stromberger (1930) | 2.46 - 13 | - | | | 9 cases. |
| Eastman (1930) | 13.3 | 6.3 | 64 | 30 | 1 case. |
| Dieckman and Kramer (1944) | 6.13 - 12.79 | 2.14 - 2.6 | | | 3 cases |

## TABLE II.

### OXYGEN IN THE UMBILICAL VESSELS OF THE HUMAN FOETUS AFTER SPONTANEOUS DELIVERY WITHOUT ANAESTHESIA

| Author. | Oxygen Content. Vols. %. Vein. | Artery. | Oxygen Saturation. %. Vein. | Remarks. |
|---|---|---|---|---|
| Blair-Bell et al (1928) | 9.0 | 5.8 | | Mean of 7 cases. |
| Goldbloom and Gottleib (1930) | 17.2 | | 79.6 | Mean of 9 cases. |
| Haselhorst and Stromberger (1930) | 4.9 - 14.9 (10.1) | 0.4 - 8 (3.4) | 45 | Mean of 22 cases. |
| Eastman (1930) | 8.2 - 13.2 (10.5) | 1.3 - 6.0 (3.3) | 50 | Mean of 10 cases. |
| Noguchi (1936) | 10.2 | 3.4 | | |

## TABLE III.

### PER CENT. SATURATION WITH OXYGEN OF BLOOD IN UMBILICAL VEIN OF HUMAN FOETUS

### SPONTANEOUS DELIVERY UNDER ANAESTHESIA (5-10 Mins).

| Author. | Ether. | Cyclopropane 75-80%. | Nitrous Oxide 20% | Pentothal 2½%. | Without Analgesia. |
|---|---|---|---|---|---|
| Smith (1939) | 57.1 | 44 | 32.6 | | |
| Taylor et al (1951) | 59.7 | 44.5 | 43 | 50.3 | |
| Watts et al (1951) | 66 | - | - | | |
| Eastman (1930) | - | - | - | - | 50 |
| Rovensteine et al (1940) | - | 8 - 35 | - | - | - |

TABLE IV.

PER CENT. SATURATION WITH OXYGEN OF BLOOD IN UMBILICAL VEIN OF HUMAN FOETUS

SPONTANEOUS DELIVERY UNDER LOCAL, SPINAL OR CAUDAL.

| Author. | Local. | Caudal. | Spinal. | Spinal. (B.P. under 90) |
|---|---|---|---|---|
| Taylor et al (1951) | 50 (26-79) | | | |
| Watts et al (1951) | | 60 | 62 | 41 |
| Batten (1943) | 46 | | 34-48 | |

TABLE V.

HAEMOGLOBIN AND RED-CELL LEVELS IN HUMAN CORD BLOOD AT BIRTH.

| Author. | No. of Cases. | Haemoglobin (g. per 100 ml.) Mean. | Haemoglobin (g. per 100 ml.) Range. | Red cells. (million per c. mm.) Mean. | Red cells. (million per c. mm.) Range. |
|---|---|---|---|---|---|
| Waugh et al (1939) | 52 | 15.36 | 11.86 - 18.72 | - | - |
| De Marsh et al (1941) | 33 | 15.80+ | 12.50 - 19.50+ | 4.51+ | 3.3 - 5.5 |
| Guest et al (1938) | 34 | 17.90 | 13 - 22 | 4.80 | 3.8 - 6.0 |
| Mugrage and Andresen (1936) | 40 | 17.14 | 13 - 20 | 4.86 | 4.0 - 5.70 |

+ Calculated from published data.

## TABLE VI.

## ANOXIA IN 530 STILLBIRTHS (MORRISON, 1952).

| Clinical Cause of Anoxia. | Number of Cases | % all Anoxia. | % Total Stillbirths. |
|---|---|---|---|
| A.P.H. | 80 | 34.5 | 15.1 |
| Labour. | 42 | 18.1 | 7.9 |
| Cord. | 34 | 14.6 | 6.4 |
| Miscell-:aneous. | 8 | 3.5 | 1.5 |
| No Cause Ascertained. | 68 | 29.3 | 12.8 |
| All Causes. | 232 | 100.0 | 43.7 |

## TABLE VII.

### BUBBLES OF VARYING LENGTH OF ATMOSPHERIC AIR ANALYSED FOR OXYGEN AND CARBON DIOXIDE

| | 1 | 2 | 3 | 4 | 5 | Mean |
|---|---|---|---|---|---|---|
| Oxygen and Carbon Dioxide | 21.5% | 21.2% | 21.5% | 20.9% | 20.5% | 21.1% (± 0.6 at most) |

## TABLE VIII.

## INCIDENCE (PER CENT.) OF DELIVERIES IN EACH WEEK OF GESTATION IN MATERNAL AGE GROUPS

| Age. | Week of Gestation. -37 | | 38 | | 39 | | 40 | | 41 | | 42 | | 43+ | | Uncertain | | Total. | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| PRIMIGRAVIDAE. | | | | | | | | | | | | | | | | | | |
| 15-19 | 52 | 9.7 | 26 | 4.9 | 50 | 9.3 | 86 | 16.0 | 105 | 19.6 | 55 | 10.3 | 34 | 6.3 | 128 | 23.8 | 536 | 100.0 |
| 20-24 | 152 | 6.7 | 117 | 5.2 | 246 | 10.9 | 422 | 18.6 | 519 | 22.9 | 323 | 14.3 | 174 | 7.7 | 311 | 13.7 | 2264 | 100.0 |
| 25-29 | 69 | 6.3 | 46 | 4.2 | 149 | 13.6 | 245 | 22.4 | 259 | 23.6 | 176 | 16.1 | 74 | 6.7 | 78 | 7.1 | 1096 | 100.0 |
| 30-34 | 20 | 6.2 | 17 | 5.3 | 28 | 8.7 | 61 | 18.9 | 105 | 32.5 | 47 | 14.6 | 22 | 6.8 | 23 | 7.1 | 323 | 100.0 |
| 35+ | 13 | 9.0 | 8 | 5.5 | 17 | 11.7 | 27 | 18.6 | 42 | 29.0 | 15 | 10.4 | 7 | 4.8 | 16 | 11.0 | 145 | 100.0 |
| All Ages. | 306 | 7.0 | 214 | 4.9 | 490 | 11.2 | 841 | 19.3 | 1030 | 23.6 | 616 | 14.1 | 311 | 7.1 | 556 | 12.8 | 4364 | 100.0 |
| MULTIGRAVIDAE. | | | | | | | | | | | | | | | | | | |
| All Ages. | 432 | 6.5 | 335 | 5.0 | 772 | 11.5 | 1382 | 20.7 | 1580 | 23.6 | 896 | 13.4 | 356 | 5.3 | 934 | 14.0 | 6687 | 100.0 |

## TABLE IX.

## HAEMOGLOBIN LEVELS AND OXYGEN CAPACITY IN CORD BLOOD OF FOETUS IN NORMAL LATE PREGNANCY.

| Weeks of Pregnancy. | Haemoglobin (g. per 100 ml.) | | Oxygen Capacity. (vols %). | |
|---|---|---|---|---|
| | Average. | Range. | Average. | Range. |
| 38 | 15.2 | 14.8 - 15.5 | 20.4 | 19.8 - 20.8 |
| 39 | 16.1 | 14.8 - 17.4 | 21.6 | 19.8 - 23.3 |
| 40 | 16.5 | 15.0 - 18.6 | 22.1 | 20.0 - 25.0 |
| 41 | 17.0 | 14.8 - 18.9 | 22.8 | 19.8 - 25.4 |
| 42 | 18.0 | 16.5 - 20.1 | 24.2 | 22.1 - 27.0 |
| 43 | 18.8 | 16.8 - 20.5 | 25.2 | 22.5 - 27.5 |

## TABLE X.

## RED-CELL COUNT IN CORD BLOOD OF FOETUS IN NORMAL LATE PREGNANCY.

| Weeks of Pregnancy. | Red Cells (million per c.mm.) | |
|---|---|---|
| | Average. | Range. |
| 38 | 4.20 | 3.52 - 4.58 |
| 39 | 4.10 | 3.71 - 4.57 |
| 40 | 4.35 | 3.74 - 4.94 |
| 41 | 4.35 | 3.71 - 5.13 |
| 42 | 4.63 | 4.10 - 5.27 |
| 43 | 4.83 | 4.40 - 5.24 |

## TABLE XI.

## OXYGEN IN BLOOD OF UMBILICAL VESSELS IN NORMAL PREGNANCY.

| Case No. | Menstrual Age (wks) | Oxygen Content. (vols. %). | | Oxygen Saturation. (%) | | Oxygen Capacity (vols. %) |
|---|---|---|---|---|---|---|
| | | Vein. | Artery. | Vein. | Artery. | |
| 1 | 21 | 12.4 | 7.9 | 66.7 | 42.4 | 18.6 |
| 2 | 22 | 12.7 | 3.9 | 68.3 | 21.0 | 18.6 |
| 3 | 22 | 14.0 | 7.4 | 74.3 | 39.4 | 18.8 |
| 4 | 22 | 13.9 | 7.3 | 72.2 | 38.0 | 19.2 |
| 5 | 29 | 12.8 | 5.7 | 67.0 | 30.0 | 19.2 |
| 6 | 30 | 13.9 | 7.1 | 67.8 | 34.8 | 20.4 |
| 7 | 39 | 12.3 | 6.0 | 56.5 | 27.2 | 21.8 |
| 8 | 39 | 11.2 | 5.0 | 56.4 | 24.8 | 19.8 |
| 9 | 40 | 12.7 | 6.7 | 57.6 | 27.1 | 22.2 |
| 10 | 40 | 12.5 | 4.9 | 61.3 | 24.0 | 20.4 |
| 11 | 40 | 10.8 | 4.6 | 54.7 | 23.0 | 19.8 |
| 12 | 40 | 10.6 | 3.1 | 52.8 | 15.8 | 20.0 |
| 13 | 42 | 9.7 | 2.8 | 43.8 | 12.6 | 22.2 |
| 14 | 42 | 8.5 | 1.6 | 37.1 | 7.2 | 22.8 |
| 15 | 42 | 9.6 | 1.8 | 41.1 | 7.6 | 23.4 |
| 16 | 42 | 7.8 | 0.7 | 29.1 | 2.5 | 26.8 |
| 17 | 43 | 8.2 | 1.9 | 32.1 | 7.4 | 25.6 |
| 18 | 43 | 6.0 | 0.9 | 22.6 | 3.4 | 26.2 |

## TABLE XII.

## OXYGEN LEVELS UMBILICAL VESSELS.

## SPONTANEOUS DELIVERY WITHOUT ANAESTHESIA AND WITHOUT EVIDENCE OF MECONIUM STAINING.

| Case No. | Menstrual Age (wks) | Duration Labour (hrs) | Oxygen Capacity vols. % | Oxygen Content in vols. %. | | Per cent. Saturation. | |
|---|---|---|---|---|---|---|---|
| | | | | Vein. | Artery. | Vein. | Artery. |
| 412/51 | 38 | 19 | 23.8 | 11.9 | 0.7 | 50.0 | 2.4 |
| 2001/52 | 39 | 38 | 19.8 | 11.8 | 5.4 | 60.0 | 28.0 |
| 2821/52 | 39 | 9 | 22.4 | 12.7 | 5.4 | 57.0 | 24.0 |
| 1642/52 | 39 | 17 | 21.8 | 12.4 | 6.2 | 56.9 | 28.5 |
| 827/51 | 41 | 12 | 22.0 | 12.2 | - | 55.3 | - |
| 806/51 | 41 | 7 | 23.0 | 11.7 | 6.3 | 50.9 | 27.6 |
| 805/51 | 41 | 12 | 23.1 | 12.2 | 6.6 | 52.8 | 28.8 |
| 813/51 | 41 | 14 | 20.6 | 8.9 | 3.6 | 42.8 | 17.4 |
| 2728/52 | 42 | 13 | 23.6 | 10.4 | 4.5 | 44.0 | 19.0 |
| 1597/51 | 43 | 11 | 23.8 | 3.2 | 0.2 | 13.4 | 0.9 |
| | | Mean: | 22.4 | 10.7 | 4.3 | 48.3 | 19.6 |

## TABLE XIII.

## OXYGEN IN BLOOD OF UMBILICAL VESSELS IN DIFFICULT LABOUR WITHOUT EVIDENCE OF MECONIUM.

| Case No. | Menstrual Age (wks) | Type of Delivery | Duration Labour (hrs) | Oxygen Capacity vols. %. | Oxygen Content vols. % | | Percent Saturation | |
|---|---|---|---|---|---|---|---|---|
| | | | | | Vein. | Artery. | Vein. | Artery. |
| 2969/50 | 39 | Low forceps | 17 | 24.2 | 13.9 | 5.3 | 57.3 | 22.0 |
| 525/51 | 40 | Low forceps | 19 | 21.6 | 11.6 | 1.0 | 53.9 | 4.1 |
| 1651/51 | 40 | Difficult mid forceps | 55 | 23.1 | 8.6 | 2.8 | 37.1 | 12.2 |
| 2820/52 | 40 | Difficult mid forceps | 89 | 22.2 | 12.1 | 6.0 | 55.0 | 27.1 |
| 2765/50 | 41 | Mid forceps | 11 | 19.8 | 10.0 | 4.0 | 50.4 | 20.1 |
| 3124/50 | 41 | LUCS | 21 | 24.2 | 13.3 | 7.3 | 54.8 | 30.0 |
| 506/51 | 43 | Difficult mid forceps | 46 | 24.8 | 6.8 | 3.6 | 27.6 | 14.5 |
| 3027/52 | 43 | LUCS | 34 | 23.4 | 6.5 | 0.9 | 28.0 | 4.0 |
| | | | Mean: | 22.9 | 10.4 | 3.9 | 45.5 | 16.8 |

## TABLE XIV.

## OXYGEN IN THE UMBILICAL VESSELS WHEN THERE IS RECENT MECONIUM STAINING.

| Case No. | Menstrual Age (wks) | Type of Delivery. | Duration Labour (hrs) | Degree of Meconium Staining. | Oxygen Capacity vols. %. | Oxygen Content vols. %. | | Percent. Saturation. | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Vein. | Artery. | Vein. | Artery. |
| 2683/50 | 40 | LUCS. | 32 | Light | 21.8 | 6.6 | Nil | 30.2 | Nil |
| 667/53 | 41 | LUCS. | 94 | Light | 27.2 | 7.5 | 1.5 | 28.2 | 5.0 |
| 2995/50 | 41 | LUCS. | 12 | V.Heavy | 22.2 | 3.9 | 0.9 | 17.6 | 4.0 |
| 1596/53 | 42 | LUCS. | Elect. | V.Heavy | 24.6 | 7.7 | 1.5 | 31.4 | 6.0 |
| 5/52 | 43 | LUCS. | 114 | V.Heavy | 25.2 | 2.0 | 0.9 | 8.0 | 3.6 |
| 1447/51 | 43 | LUCS. | 18 | V.Heavy | 23.2 | 4.3 | 0.5 | 18.7 | 2.0 |
| 2291/51 | 43 | LUCS. | 49 | Light | 25.8 | 5.4 | 0.7 | 20.8 | 2.6 |
| 991/51 | 43 | LUCS. | 62 | Moderate | 25.6 | 3.0 | 0.7 | 11.6 | 2.6 |
| 3054/52 | 43 | LUCS | 35 | Moderate | 25.6 | 6.6 | 2.0 | 25.8 | 7.8 |
| 1506/51 | 43 | S.D. | 16 | Light | 24.6 | 7.5 | 3.7 | 30.6 | 11.9 |
| 3001/51 | 43 | LUCS. | Elect. | Light | 25.6 | 8.2 | 1.9 | 32.1 | 7.4 |
| | | | | Mean: | 24.7 | 5.7 | 1.3 | 23.2 | 4.8 |

TABLE XV.

OXYGEN IN BLOOD OF UMBILICAL VESSELS IN PRE-ECLAMPSIA.

| Case No. | Menstrual Age (wks) | Severity of disease | Oxygen Content (vols. %.) Vein. | Artery. | Oxygen Saturation (%). Vein. | Artery. | Oxygen Capacity. (vols. %). |
|---|---|---|---|---|---|---|---|
| 19 | 34 | Severe | 5.6 | 2.9 | 22.5 | 11.5 | 25.0 |
| 20 | 35 | Severe | 4.8 | 1.5 | 21.4 | 6.9 | 22.3 |
| 21 | 35 | Severe | 6.8 | 2.9 | 31.4 | 13.2 | 21.8 |
| 22 | 36 | Severe | 2.6 | Nil | 10.5 | .. | 25.0 |
| 23 | 37 | Moderate | 10.4 | 4.6 | 46.8 | 20.8 | 22.2 |
| 24 | 39 | Severe | 8.0 | 1.4 | 32.5 | 5.5 | 24.8 |

TABLE XVI.

OXYGEN LEVELS IN UMBILICAL VESSELS AT ELECTIVE CAESAREAN SECTION.

CASES WITH STILLBIRTH OR EARLY NEONATAL DEATH (OBSTETRIC DEATH) IN THE IMMEDIATELY PRECEDING PREGNANCY.

| Case No. | Menstrual Age (wks). | Time of Previous O.D. (wks) | Oxygen Capacity. vols. % | Oxygen Content. vols. % Vein. | Oxygen Content. vols. % Artery. | Oxygen Saturation. % Vein. | Oxygen Saturation. % Artery. |
|---|---|---|---|---|---|---|---|
| 194/51 | 36 | 35 | 21.8 | 8.3 | - | 37.9 | - |
| 2695/52 | 38 | 36: 39 | 20.2 | 9.4 | 1.3 | 47.0 | 6.6 |
| 2820/50 | 39 | 34 | 24.4 | 8.5 | 1.1 | 34.8 | 4.8 |
| 2463/51 | 40 | 40 | 27.8 | 10.4 | 4.3 | 37.4 | 15.4 |
| 1665/51 | 40 | 40 | 24.2 | 6.0 | 1.4 | 24.7 | 5.7 |
| 1260/50 | 40 | 25: 26:27 | 27.8 | 8.8 | - | 31.7 | - |
| 193/52 | 40 | 30 | 23.6 | 11.5 | 3.6 | 48.7 | 15.3 |
| 2959/50 | 39 | 41:42 | 25.2 | 13.8 | 5.8 | 55.0 | 23.0 |
| 2195/52 | 39 | 43 | 24.2 | 11.1 | 5.7 | 45.9 | 23.5 |
| 553/51 | 40 | 43 | 23.4 | 9.1 | 3.2 | 39.1 | 13.6 |
| 563/51 | 42 | 43 | 27.6 | 7.5 | 1.2 | 27.0 | 4.1 |
| | | Mean: | 24.6 | 9.5 | 3.1 | 39.0 | 12.4 |

## TABLE XVII.

### RELATION OF HAEMOGLOBIN LEVEL IN CORD BLOOD TO OXYGEN CONTENT AND SATURATION OF BLOOD IN UMBILICAL VEIN BEFORE ONSET OF LABOUR

| Haemoglobin. (g. per 100 ml.) | Haemoglobin. (%) | Oxygen Capacity (vols. %.) | No. of Cases. | Mean oxygen content of vein. (vols.%.) | Mean oxygen saturation of vein (vols. %). |
|---|---|---|---|---|---|
| - 14.8 | - 100 | - 20 | 6 | 12.5 | 65.4 |
| 14.9-16.3 | 101-110 | 20-22 | 6 | 10.6 | 50.5 |
| 16.4-17.8 | 111-120 | 22-24 | 8 | 9.6 | 42.0 |
| 17.9+ | 121+ | 24+ | 16 | 7.8 | 31.9 |

This table is compiled from the results of 36 cases in which haemoglobin and oxygen estimations were made before the onset of labour. It therefore includes normal and abnormal pregnancies at all stages of gestation and is designed solely to demonstrate the relation between oxygen capacity, oxygen content, and percentage saturation.

## TABLE XVIII.

### OXYGEN IN BLOOD OF UMBILICAL VESSELS SHOWING HIGH CAPACITY AT 40 WEEKS

| Case No. | Menstrual Age (wks.) | Oxygen Content. (vols. %.) Vein. | Oxygen Content. (vols. %.) Artery. | Oxygen Satur-:ation (%) Vein. | Oxygen Satur-:ation (%) Artery. | Oxygen Capacity. Vols. % |
|---|---|---|---|---|---|---|
| 25 | 40 | 6.8 | 1.8 | 31.1 | 6.0 | 25.0 |

## TABLE XIX.

## OXYGEN LEVELS IN BLOOD OF UMBILICAL VESSELS

## NORMAL PREGNANCY AT CAESAREAN SECTION UNDER SPINAL ANALGESIA BEFORE ONSET OF LABOUR.

## MATERNAL SYSTOLIC BLOOD PRESSURE DROPPED BELOW 80 m.m. OF MERCURY.

| Case No. | Menstrual Age. (wks) | Oxygen Capacity. | Percent. Saturation Vein. Percentage Expected. | Found. |
|---|---|---|---|---|
| 2924/53 | 36 | 21.2 | 45 - 55 | 33.8 |
| 2534/51 | 41 | 22.2 | 40 - 50 | 30.1 |
| 1354/51 | 41 | 22.8 | 40 - 50 | 27.6 |

## TABLE XX.

## OXYGEN LEVELS IN THE UMBILICAL VESSELS

### NORMAL PREGNANCY AT CAESAREAN SECTION UNDER SPINAL ANAESTHESIA BEFORE THE ONSET OF LABOUR WHERE EXTRACTION OF THE FOETUS WAS DIFFICULT OR WHERE THE UMBILICAL CORD WAS INTERFERED WITH

| Case No. | Menstrual Age (wks) | Oxygen Capacity. | Percent. Saturation Vein. Percentage | |
|---|---|---|---|---|
| | | | Expected. | Found. |
| 1246/51 | 40 | 22.2 | 40 - 50 | 40 |
| 354/52 | 40 | 23.4 | 40 - 45 | 27 |
| 1053/51 | 41 | 24.2 | 30 - 40 | 28.9 |

## TABLE XXI.

### OBSTETRIC DEATH RATES PER 1000 TOTAL BIRTHS.

### CLINICAL CAUSE GROUPS BY PARITY WITH SUBDIVISION OF TRAUMA AND PRESENTATION OF THE GROUP DUE TO DIFFICULT LABOUR (VERTEX PRESENTATION).

| Parity. | 1. | | 2. | | 3. | | 4-6 | | 7+ | | All Preg. | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Type of Death. | Cases | Rates. | Cases. | Rates. | Cases | Rates. | Cases | Rates. | Cases | Rates. | Cases | Rates. |
| M.U. | 67 | 6.2 | 32 | 4.9 | 15 | 4.8 | 10 | 4.1 | 3 | 5.0 | 127 | 5.4 |
| Tr. | 80 | 7.4 | 35 | 5.3 | 14 | 4.5 | 9 | 3.6 | 8 | 13.4 | 146 | 6.2 |
| Str.A. | 30 | 2.8 | 4 | 0.6 | 2 | 0.6 | 1 | 0.4 | 1 | 1.7 | 38 | 1.6 |
| P.U. | 83 | 7.7 | 36 | 5.5 | 29 | 9.3 | 25 | 10.1 | 6 | 10.1 | 179 | 7.6 |
| Tox. | 53 | 4.9 | 21 | 3.2 | 9 | 2.9 | 7 | 2.8 | 3 | 5.0 | 93 | 4.0 |
| A.P.H. | 37 | 3.4 | 24 | 3.7 | 14 | 4.5 | 18 | 7.3 | 10 | 16.8 | 103 | 4.4 |
| Def. | 79 | 7.3 | 32 | 4.9 | 15 | 4.8 | 12 | 4.9 | 5 | 8.4 | 143 | 6.1 |
| M.D. | 25 | 2.3 | 18 | 2.7 | 5 | 1.6 | 6 | 2.4 | 4 | 6.7 | 58 | 2.5 |
| All Others | 10 | 0.9 | 9 | 1.4 | 12 | 3.8 | 11 | 4.5 | 2 | 3.4 | 44 | 1.9 |
| TOTAL. | 464 | 43.1 | 211 | 32.2 | 115 | 36.8 | 99 | 40.1 | 42 | 70.4 | 931 | 39.6 |
| No. of Cases | 10758 | | 6547 | | 3124 | | 2466 | | 597 | | 23492 | |
| Trauma. | | | | | | | | | | | | |
| Diff.Vertex | 35 | 3.3 | 6 | 0.9 | 3 | 1.0 | 2 | 0.8 | 1 | 1.7 | 47 | 2.0 |
| Other Trauma (Malpres. Cord) | 45 | 4.1 | 29 | 4.4 | 11 | 3.5 | 7 | 2.8 | 7 | 11.7 | 99 | 4.2 |
| Diff.Labour. Vertex Pres. | | | | | | | | | | | | |
| Diff.Vertex | 35 | 3.3 | 6 | 0.9 | 3 | 1.0 | 2 | 0.8 | 1 | 1.7 | 47 | 2.0 |
| Str.A. | 30 | 2.8 | 4 | 0.6 | 2 | 0.6 | 1 | 0.4 | 1 | 1.7 | 38 | 1.6 |

## TABLE XXII.

### OBSTETRIC DEATH RATES PER 1000 TOTAL BIRTHS.
### SOME CLINICAL CAUSES BY MATERNAL AGE IN PRIMIGRAVIDAE

| Type of Death. | 15-19 | | 20-24 | | 25-29 | | 30-34 | | 35+ | | All Ages. | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| M.U. | 4 | 2.5 | 23 | 4.4 | 17 | 6.6 | 14 | 15.6 | 9 | 20.4 | 67 | 6.2 |
| Str.A. | 2 | 1.2 | 8 | 1.5 | 14 | 5.4 | 4 | 4.5 | 2 | 4.5 | 30 | 2.8 |
| Trauma. | | | | | | | | | | | | |
| Diff.Vertex | 3 | 1.9 | 17 | 3.2 | 6 | 2.3 | 7 | 7.8 | 2 | 4.5 | 35 | 3.3 |
| Other Trauma. | 5 | 3.1 | 22 | 4.2 | 7 | 2.7 | 7 | 7.8 | 4 | 9.1 | 44 | 4.1 |
| Tox. | 12 | 7.5 | 13 | 2.5 | 10 | 3.9 | 9 | 10.0 | 9 | 20.4 | 53 | 4.9 |
| Total Deaths | 59 | 36.7 | 178 | 34.0 | 124 | 48.1 | 63 | 70.2 | 40 | 90.7 | 464 | 43.1 |
| Cases at Risk. | 1606 | | 5235 | | 2578 | | 898 | | 441 | | 10758 | |
| Difficult Labour. Diff.Vertex) and Str.A. ) | 5 | 3.1 | 25 | 4.7 | 20 | 7.7 | 11 | 12.3 | 4 | 9.0 | 65 | 6.1 |

## TABLE XXIII.

### OBSTETRIC DEATH RATES PER 1000 TOTAL BIRTHS.
### SOME CLINICAL CAUSES BY MATERNAL AGE IN MULTIGRAVIDAE.

| Type of Death. | 15-19 | | 20-24 | | 25-29 | | 30-34 | | 35+ | | All Ages. | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| M.U. | - | | 11 | 3.5 | 17 | 3.9 | 16 | 5.4 | 16 | 7.7 | 60 | 4.7 |
| Str.A. | - | | 2 | 0.6 | - | | 3 | 1.0 | 3 | 1.4 | 8 | 0.6 |
| **Trauma.** | | | | | | | | | | | | |
| Diff.Vertex | - | | 1 | 0.3 | 3 | 0.7 | 1 | 0.3 | 7 | 3.4 | 12 | 0.9 |
| Other Trauma | 1 | 4.7 | 9 | 2.9 | 10 | 2.3 | 16 | 5.4 | 18 | 8.7 | 54 | 4.2 |
| **Tox.** | 2 | 9.3 | 5 | 1.6 | 8 | 1.8 | 13 | 4.4 | 12 | 5.8 | 40 | 3.1 |
| Total Deaths | 7 | 32.7 | 96 | 30.9 | 131 | 29.8 | 107 | 36.4 | 124 | 59.6 | 467 | 36.7 |
| Cases at Risk | 214 | | 3103 | | 4399 | | 2939 | | 2079 | | 12734 | |
| Difficult Labour: Diff.Vertex and StrA. | - | | 3 | 0.9 | 3 | 0.7 | 4 | 1.3 | 10 | 4.8 | 20 | 1.5 |

## TABLE XXIV.

## PRIMIGRAVIDAE - STILLBIRTH, FIRST WEEK AND OBSTETRIC DEATH RATE PER 1000 TOTAL BIRTHS.

| | Week of Delivery - Menstrual Age | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | - 37 | | 38-39 | | 40 | | 41 | | 42 | | 43+ | | Uncertain | | Total | |
| Stillbirths | 33 | 107.8 | 13 | 18.5 | 8 | 9.5 | 8 | 7.8 | 8 | 13.0 | 9 | 28.9 | 16 | 28.8 | 95 | 21.8 |
| 1st week Deaths | 35 | 114.4 | 6 | 8.5 | 5 | 5.9 | 4 | 3.9 | 5 | 8.1 | 3 | 9.6 | 8 | 14.4 | 66 | 15.1 |
| Obstetric Deaths | 68 | 222.2 | 19 | 27.0 | 13 | 15.5 | 12 | 11.7 | 13 | 21.1 | 12 | 38.6 | 24 | 43.2 | 161 | 36.9 |
| Obstetric Deaths: | | | | | | | | | | | | | | | | |
| M.U. | 1 | 3.3 | 3 | 4.3 | 3 | 3.6 | 5 | 4.9 | 4 | 6.5 | 6 | 19.3 | 2 | 3.6 | 24 | 5.5 |
| Difficult Labour: | | | | | | | | | | | | | | | | |
| Diff. Vertex) and StrA. ) | - | | 3 | 4.3 | 1 | 1.2 | - | | 5 | 8.1 | 2 | 6.4 | 1 | 1.8 | 12 | 2.7 |
| Others | 67 | 218.9 | 13 | 18.4 | 9 | 10.7 | 7 | 6.8 | 4 | 6.5 | 4 | 12.9 | 21 | 37.8 | 125 | 28.7 |
| Cases at Risk | 306 | | 704 | | 841 | | 1030 | | 616 | | 311 | | 556 | | 4364 | |

## TABLE XXV.

## MULTIGRAVIDAE - STILLBIRTH, FIRST WEEK AND OBSTETRIC DEATH RATE PER 1000 TOTAL BIRTHS BY WEEK OF DELIVERY.

| | Week of Delivery | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | -37 | | 38-39 | | 40 | | 41 | | 42 | | 43+ | | Uncertain | | Total | |
| Stillbirths | 48 | 111.1 | 14 | 12.7 | 8 | 5.8 | 12 | 7.6 | 12 | 13.4 | 6 | 16.9 | 19 | 20.3 | 119 | 17.8 |
| 1st week Deaths | 35 | 81.0 | 9 | 8.1 | 5 | 3.6 | 6 | 3.8 | 4 | 4.5 | 2 | 5.6 | 11 | 11.8 | 72 | 10.8 |
| Obstetric Deaths | 83 | 192.1 | 23 | 20.8 | 13 | 9.4 | 18 | 11.4 | 16 | 17.9 | 8 | 22.5 | 30 | 32.1 | 191 | 28.6 |
| Obstetric Deaths: | | | | | | | | | | | | | | | | |
| M.U. | 1 | 2.3 | 4 | 3.6 | 2 | 1.4 | 7 | 4.4 | 7 | 7.8 | 3 | 8.4 | 3 | 3.2 | 27 | 4.0 |
| Difficult Labour: | | | | | | | | | | | | | | | | |
| Diff. Vertex) and StrA. ) | - | | 1 | 0.9 | 2 | 1.4 | 1 | 0.6 | 1 | 1.1 | 2 | 5.6 | - | | 7 | 1.0 |
| Others | 82 | 189.8 | 18 | 16.3 | 9 | 6.6 | 10 | 6.4 | 8 | 9.0 | 3 | 8.5 | 27 | 28.9 | 157 | 23.6 |
| Cases at Risk | 432 | | 1107 | | 1382 | | 1580 | | 896 | | 356 | | 934 | | 6687 | |

## TABLE XXVI.

OBSTETRIC DEATH - PROPORTION (PER CENT.) OF DEATHS DUE TO SOME CLINICAL CAUSES BY WEEKS OF DELIVERY.

| | Week of Delivery. | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | -37 | | 38-39 | | 40 | | 41 | | 42+ | | Uncertain. | | Totals. | |
| **PRIMIGRAVIDAE.** | | | | | | | | | | | | | | |
| M.U. | 3 | 1.7 | 8 | 11.3 | 5 | 16.7 | 11 | 24.4 | 34 | 32.4 | 6 | 15.0 | 67 | 14.4 |
| Difficult Labour: StrA. | - | | - | | 1 | 3.3 | 3 | 6.7 | 25 | 23.8 | 1 | 2.5 | 30 | 6.5 |
| Diff.Vertex. | - | | 11 | 15.5 | 4 | 13.3 | 4 | 8.8 | 14 | 13.3 | 2 | 5.0 | 35 | 7.5 |
| Total Deaths | 173 | | 71 | | 30 | | 45 | | 105 | | 40 | | 464 | |
| **MULTIGRAVIDAE.** | | | | | | | | | | | | | | |
| M.U. | 4 | 1.8 | 11 | 19.6 | 3 | 11.5 | 16 | 30.2 | 21 | 35.6 | 5 | 11.1 | 60 | 12.8 |
| Difficult Labour: StrA. | - | | 1 | 1.8 | - | | 1 | 1.9 | 6 | 10.2 | - | | 8 | 1.7 |
| Diff.Vertex. | - | | 2 | 3.6 | 3 | 11.5 | 5 | 9.4 | 2 | 3.4 | - | | 12 | 2.6 |
| Total Deaths | 228 | | 56 | | 26 | | 53 | | 59 | | 45 | | 467 | |

## TABLE XXVII.

## CAUSE OF OBSTETRIC DEATH AFTER THE 41st WEEK OF PREGNANCY IN 10758 PRIMIGRAVIDAE.

| Cause | | | Per cent. |
|---|---|---|---|
| Difficult Labour (Vertex) | Anoxia | 23.8 | 48.5 |
| | Trauma | 13.3 | |
| Malpresentation; | Cord | 11.4 | |
| Deformity | | | 7.6 |
| Unexplained (Mature) | | 32.4 | 43.9 |
| Toxaemia | | 4.8 | |
| Other | | 6.7 | |
| TOTAL. | | | 100.0 (105 cases) |

## TABLE XXVIII.

## INCIDENCE OF FOETAL DISTRESS IN VARIOUS TYPES OF LABOUR IN PRIMIGRAVIDAE

| | Week of Delivery. | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | -37 | 38-39 | 40 | 41 | 42 | 43 | 44+ | Uncertain | Total |
| All Labours | 254 | 573 | 693 | 813 | 501 | 200 | 58 | 412 | 3504 |
| Cases of Distress | 15 | 49 | 58 | 122 | 113 | 48 | 15 | 48 | 468 |
| % Incidence | 5.9 | 8.6 | 8.4 | 15.0 | 22.6 | 24.0 | 25.9 | 11.7 | 13.4 |
| All Difficult Labour (Vertex) | 39 | 114 | 168 | 242 | 162 | 71 | 20 | 90 | 906 |
| Cases of Distress | 3 | 19 | 22 | 65 | 57 | 28 | 7 | 23 | 224 |
| % Incidence | 7.7 | 16.7 | 13.1 | 26.9 | 35.2 | 39.4 | 35.0 | 25.6 | 24.7 |
| Non-Difficult Labour (exc. malpresentations) | 194 | 442 | 515 | 554 | 330 | 123 | 38 | 307 | 2503 |
| Cases of Distress | 11 | 29 | 35 | 53 | 52 | 17 | 8 | 24 | 229 |
| % Incidence | 5.7 | 6.6 | 6.8 | 9.6 | 15.8 | 13.8 | 21.1 | 7.8 | 9.1 |

## TABLE XXIX.

### FOETAL DISTRESS - PRIMIGRAVIDAE
### NUMBER OF CASES AND INCIDENCE OF DISTRESS IN ALL DELIVERIES BY CAUSE OF DISTRESS BY WEEK IN WHICH DELIVERY OCCURRED

| | -37 | | 38 | | 39 | | 40 | | 41 | | 42 | | 43 | | 44+ | | Uncertain | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Total number of cases | 254 | | 175 | | 398 | | 693 | | 813 | | 501 | | 200 | | 58 | | 412 | | 3504 | |
| A.P.H. | 1 | 0.4 | - | | 2 | 0.5 | 1 | 0.1 | 1 | 0.1 | - | | 1 | 0.5 | - | | - | | 6 | 0.2 |
| Tox. | 3 | 1.2 | 1 | 0.6 | 3 | 0.8 | 5 | 0.7 | 1 | 0.1 | 1 | 0.2 | 1 | 0.5 | - | | 2 | 0.5 | 17 | 0.5 |
| Cord | - | | 1 | 0.6 | 8 | 2.0 | 10 | 1.4 | 18 | 2.2 | 16 | 3.2 | 5 | 2.5 | 2 | 3.4 | 5 | 1.2 | 65 | 1.9 |
| Pressure on head. | 1 | 0.4 | - | | 6 | 1.5 | 5 | 0.7 | 15 | 1.8 | 17 | 3.4 | 7 | 3.5 | - | | 2 | 0.5 | 53 | 1.5 |
| 2nd Stage | 7 | 2.8 | 5 | 2.9 | 9 | 2.3 | 21 | 3.0 | 38 | 4.7 | 24 | 4.8 | 9 | 4.5 | 3 | 5.2 | 10 | 2.4 | 126 | 3.6 |
| Prolonged Labour | - | | 1 | 0.6 | 2 | 0.5 | 3 | 0.4 | 8 | 1.0 | 12 | 2.4 | 4 | 2.0 | 3 | 5.2 | 5 | 1.2 | 38 | 1.1 |
| Cause Unknown | - | | 3 | 1.7 | 8 | 2.0 | 11 | 1.6 | 37 | 4.6 | 39 | 7.8 | 21 | 10.5 | 6 | 10.3 | 21 | 5.1 | 146 | 4.2 |
| Others | 3 | 1.2 | - | | - | | 2 | 0.3 | 4 | 0.5 | 4 | 0.8 | - | | 1 | 1.7 | 3 | 0.7 | 17 | 0.5 |
| Total: Meconium | 3 | 1.2 | 4 | 2.3 | 16 | 4.0 | 28 | 4.0 | 61 | 7.5 | 67 | 13.4 | 28 | 14.0 | 10 | 17.2 | 28 | 6.8 | 245 | 7.0 |
| Heart | 12 | 4.7 | 7 | 4.0 | 22 | 5.5 | 30 | 4.3 | 61 | 7.5 | 46 | 9.2 | 20 | 10.0 | 5 | 8.6 | 20 | 4.8 | 223 | 6.4 |
| All Cases. | 15 | 5.9 | 11 | 6.3 | 38 | 9.5 | 58 | 8.4 | 122 | 15.0 | 113 | 22.6 | 48 | 24.0 | 15 | 25.9 | 48 | 11.7 | 468 | 13.4 |

TABLE XXX.

FOETAL DISTRESS - MULTIGRAVIDAE
NUMBER OF CASES AND INCIDENCE OF DISTRESS IN ALL DELIVERIES
BY CAUSE OF DISTRESS BY WEEKS IN WHICH DELIVERY OCCURRED

| | -37 | | 38-39 | | 40 | | 41 | | 42 | | 43+ | | Uncertain | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Total Number of Cases | 360 | | 881 | | 1112 | | 1269 | | 684 | | 314 | | 692 | | 5312 | |
| Tox. and A.P.H. | 2 | 0.6 | 3 | 0.3 | 2 | 0.2 | 1 | 0.1 | 2 | 0.3 | - | | 5 | 0.7 | 15 | 0.3 |
| Cord | 7 | 1.9 | 6 | 0.7 | 9 | 0.8 | 13 | 1.0 | 4 | 0.6 | 3 | 1.0 | 6 | 0.9 | 48 | 0.9 |
| Cause Unknown | 9 | 2.5 | 20 | 2.3 | 47 | 4.2 | 66 | 5.2 | 57 | 8.3 | 22 | 7.0 | 45 | 6.5 | 266 | 5.0 |
| Prolonged Labour and Pressure. | 1 | 0.3 | 8 | 0.9 | 14 | 1.3 | 12 | 0.9 | 11 | 1.6 | 2 | 0.6 | 5 | 0.7 | 53 | 1.0 |
| 2nd Stage | 1 | 0.3 | 7 | 0.8 | 9 | 0.8 | 17 | 1.3 | 5 | 0.7 | 8 | 2.5 | 4 | 0.6 | 51 | 1.0 |
| Other | 1 | 0.3 | 5 | 0.6 | 3 | 0.3 | 2 | 0.2 | 1 | 0.1 | 3 | 1.0 | 2 | 0.3 | 17 | 0.3 |
| Total: | | | | | | | | | | | | | | | | |
| Meconium | 11 | 3.1 | 33 | 3.7 | 62 | 5.6 | 82 | 6.5 | 67 | 9.8 | 27 | 8.6 | 54 | 7.8 | 336 | 6.3 |
| Heart | 10 | 2.8 | 16 | 1.8 | 22 | 2.0 | 29 | 2.3 | 13 | 1.9 | 11 | 3.5 | 13 | 1.9 | 114 | 2.1 |
| All Cases. | 21 | 5.8 | 49 | 5.6 | 84 | 7.6 | 111 | 8.7 | 80 | 11.7 | 38 | 12.1 | 67 | 9.7 | 450 | 8.5 |

## TABLE XXXI.

## FOETAL DISTRESS - "UNKNOWN CAUSE" - PERCENT. INCIDENCE.

| | Week of Delivery. | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | -37 | 38-39 | 40 | 41 | 42 | 43+ | Uncertain. | Total. |
| Primigravidae. | - | 1.9 | 1.6 | 4.6 | 7.8 | 10.5 | 5.1 | 4.2 |
| Total Labours. | 254 | 573 | 693 | 813 | 501 | 258 | 412 | 3504 |
| Multigravidae. | 2.5 | 2.3 | 4.2 | 5.2 | 8.3 | 7.0 | 6.5 | 5.0 |
| Total Labours. | 360 | 881 | 1112 | 1269 | 684 | 314 | 692 | 5312 |

## TABLE XXXII.

## INCIDENCE OF MECONIUM IN FOETAL DISTRESS DUE TO VARIOUS CLINICAL CAUSES

| | Primigravidae. % showing meconium. | Multigravidae. % showing meconium. |
|---|---|---|
| Cause Unknown | 95.2 | 96.5 |
| Prolonged Labour | 71.1 | 45.0 |
| Pressure | 42.4 | |
| 2nd Stage | 5.6 | 2.0 |
| Cord | 49.2 | 66.0 |
| All Others | 42.0 | 63.0 |
| Total | 52.4 | 66 |

TABLE XXXIII.

FOETAL DISTRESS - PRIMIGRAVIDAE
INCIDENCE BY MATERNAL AGE AND TYPE OF LABOUR

| | 15-19 | 20-24 | 25-29 | 30-34 | 35+ | Total |
|---|---|---|---|---|---|---|
| Total Cases | 448 | 1797 | 877 | 261 | 121 | 3504 |
| All cases of Distress | 38 | 202 | 143 | 50 | 35 | 468 |
| % Incidence | 8.5 | 11.2 | 16.3 | 19.2 | 28.9 | 13.4 |
| All Difficult Labour (Vertex) | 72 | 381 | 287 | 107 | 59 | 906 |
| Cases of Distress | 19 | 85 | 64 | 32 | 24 | 224 |
| % Incidence | 26.4 | 22.3 | 22.3 | 29.9 | 40.7 | 24.7 |
| All non-difficult labour (excluding abnormal presentations) | 362 | 1377 | 560 | 150 | 54 | 2503 |
| Cases of Distress | 16 | 111 | 75 | 18 | 9 | 229 |
| % Incidence | 4.4 | 8.1 | 13.4 | 12.0 | 16.7 | |

## TABLE XXXIV.

### FOETAL DISTRESS - MULTIGRAVIDAE.
### INCIDENCE BY MATERNAL AGE AND TYPE OF LABOUR.

| | 15-19 | 20-24 | 25-29 | 30-34 | 35+ | Total. |
|---|---|---|---|---|---|---|
| **2nd Pregnancies.** | | | | | | |
| Total Cases | 81 | 966 | 1160 | 481 | 221 | 2909 |
| All cases of Distress | 6 | 63 | 99 | 52 | 29 | 249 |
| % Incidence | 7.4 | 6.5 | 8.5 | 10.8 | 13.1 | 8.6 |
| **3rd + Pregnancies.** | | | | | | |
| Total Cases | 9 | 404 | 825 | 631 | 534 | 2403 |
| All cases of Distress | 1 | 31 | 50 | 52 | 67 | 201 |
| % Incidence | 11.1 | 7.7 | 6.1 | 8.2 | 12.5 | 8.4 |

TABLE XXXV.

FOETAL DISTRESS - INCIDENCE BY TYPE OF DISTRESS BY MATERNAL AGE.

| | 15-19 | 20-24 | 25-29 | 30-34 | 35+ | Total. |
|---|---|---|---|---|---|---|
| PRIMIGRAVIDAE. | | | | | | |
| All Cases | 448 | 1797 | 877 | 261 | 121 | 3504 |
| Meconium | 20 | 104 | 71 | 26 | 14 | 245 |
| % Incidence | 4.5 | 5.8 | 8.1 | 9.9 | 19.8 | 7.0 |
| Heart only | 18 | 98 | 72 | 24 | 11 | 223 |
| % Incidence | 4.0 | 5.5 | 8.2 | 9.2 | 9.1 | 6.4 |
| All Distress | 38 | 202 | 143 | 50 | 35 | 468 |
| % Incidence | 8.5 | 11.2 | 16.3 | 19.2 | 28.9 | 13.4 |
| MULTIGRAVIDAE: | | | | | | |
| All Cases | 90 | 1370 | 1985 | 1112 | 755 | 5312 |
| Meconium | 5 | 66 | 114 | 80 | 71 | 336 |
| % Incidence | 5.6 | 4.8 | 5.7 | 7.2 | 9.4 | 6.3 |
| Heart only | 2 | 28 | 35 | 24 | 25 | 114 |
| % Incidence | 2.2 | 2.0 | 1.8 | 2.2 | 3.3 | 2.1 |
| All Distress | 7 | 94 | 149 | 104 | 96 | 450 |
| % Incidence | 7.8 | 6.9 | 7.5 | 9.4 | 12.7 | 8.5 |

TABLE XXXVI.

FOETAL DISTRESS IN PRIMIGRAVIDAE.
INCIDENCE BY WEEK OF DELIVERY IN VARIOUS AGE GROUPS BY TYPE OF LABOUR.

| | | -39 | 40 | 41 | 42 | 43+ | Uncertain | Total |
|---|---|---|---|---|---|---|---|---|
| 15-19 | | | | | | | | |
| All Cases. | Total Labours | 110 | 74 | 90 | 45 | 31 | 98 | 448 |
| | Cases of Distress | 10 | 3 | 8 | 3 | 4 | 10 | 38 |
| | % Incidence | 9.1 | 4.1 | 8.9 | 6.7 | 12.9 | 10.2 | 8.5 |
| All Non-Difficult Labour. | Total Labours | 85 | 63 | 70 | 40 | 24 | 81 | 363 |
| | Cases of Distress | 5 | 2 | 1 | 3 | 1 | 4 | 16 |
| | % Incidence | 5.9 | 3.2 | 1.4 | 7.5 | 4.2 | 4.9 | 4.4 |
| 20-24. | | | | | | | | |
| All Cases. | Total Labours | 421 | 354 | 395 | 259 | 143 | 225 | 1797 |
| | Cases of Distress | 22 | 26 | 46 | 51 | 30 | 25 | 200 |
| | % Incidence | 5.2 | 7.3 | 11.6 | 19.7 | 21.0 | 11.1 | 11.1 |
| All Non-Difficult Labour. | Total Labours | 342 | 282 | 298 | 181 | 99 | 175 | 1377 |
| | Cases of Distress | 18 | 16 | 25 | 27 | 13 | 12 | 111 |
| | % Incidence | 5.0 | 5.7 | 8.4 | 14.9 | 13.1 | 6.9 | 8.1 |
| 25-29. | | | | | | | | |
| All Cases. | Total Labours | 216 | 197 | 202 | 141 | 61 | 60 | 877 |
| | Cases of Distress | 27 | 21 | 30 | 39 | 20 | 7 | 144 |
| | % Incidence | 12.5 | 10.7 | 14.9 | 27.7 | 32.8 | 11.7 | 16.4 |
| All Non-Difficult Labour. | Total Labours. | 158 | 133 | 124 | 83 | 27 | 35 | 560 |
| | Cases of Distress | 15 | 14 | 14 | 19 | 8 | 5 | 75 |
| | % Incidence | 9.5 | 10.5 | 11.3 | 22.9 | 29.6 | 14.3 | 13.4 |

TABLE XXXVI. (contd).

FOETAL DISTRESS IN PRIMIGRAVIDAE.

INCIDENCE BY WEEK OF DELIVERY IN VARIOUS AGE GROUPS BY TYPE OF LABOUR.

| | | -39 | 40 | 41 | 42 | 43+ | Uncertain | Total. |
|---|---|---|---|---|---|---|---|---|
| 30-34. | | | | | | | | |
| All Cases. | Total Labours | 51 | 45 | 91 | 42 | 17 | 15 | 261 |
| | Cases of Distress | 1 | 5 | 25 | 13 | 5 | 3 | 52 |
| | % Incidence | 2.0 | 11.1 | 27.5 | 31.0 | 29.4 | 20.0 | 19.9 |
| All Non-Difficult Labour. | Total Labours | 37 | 28 | 45 | 21 | 9 | 10 | 150 |
| | Cases of Distress | 1 | 3 | 8 | 3 | 2 | 1 | 18 |
| | % Incidence | 2.7 | 10.7 | 17.8 | 14.3 | 22.2 | 10.0 | 12.0 |
| 35+. | | | | | | | | |
| All Cases. | Total Labours | 29 | 23 | 35 | 14 | 6 | 14 | 121 |
| | Cases of Distress | 4 | 3 | 13 | 7 | 4 | 3 | 34 |
| | % Incidence | 13.8 | 13.0 | 37.1 | 50.0 | 66.6 | 21.4 | 28.1 |
| All Non-Difficult Labour. | Total Labours | 14 | 10 | 17 | 5 | 2 | 6 | 54 |
| | Cases of Distress | 1 | - | 5 | - | 1 | 2 | 9 |
| | % Incidence | 5.9 | -- | 29.4 | - | 50.0 | 33.3 | 16.7 |

## TABLE XXXVII

## THE OXYGEN LEVELS IN THE VARIOUS VESSELS OF THE HUMAN FOETUS

### The Saturation in the Umbilical Vein and Abdominal Aorta (Umbilical Artery) from the Oxygen Findings of this Thesis

| Clinical State | Umbilical Vein. | | Carotid Estimated. | | Umbilical Artery. (Abdominal Aorta). | |
|---|---|---|---|---|---|---|
| Weeks. | Saturation | Tension | Saturation | Tension | Saturation | Tension. |
| 30 | 70 | 32 | 60 | 28 | 35 | 22 |
| 40 | 60 | 30 | 45 | 22 | 30 | 18 |
| | 50 | 25 | 35 | 20 | 20 | 15 |
| 43 | 40 | 20 | 25 | 18 | 10 | 10 |
| Distress | 30 | 18 | 15-20 | 14-16 | Nil | Nil |

Other saturations estimated (Carotid, Barcroft et al, 1938 and 1939)
The tensions at 30 weeks from the dissociation curve of Sachs and Likhnizkaya (1938); Fig. 22.
The tensions at other periods from the dissociation curve of Eastman et al (1933); Fig. 21.
(Assuming that dissociation curve is unaltered by increased concentration of haemoglobin or by lowered pH in anoxia).

# (3) ILLUSTRATIVE CLINICAL CASE HISTORIES.

CASE NO. 1.

## TYPICAL MATURE UNEXPLAINED STILLBIRTH IN PRIMIGRAVIDA.

2406/53. Primigravida. Aged 23.

Attended ante natal clinic from 21st week.

| Weeks. | Maternal Weight. |
|---|---|
| 21 | 124¼ lb. |
| 25 | 127¼ lb. |
| 29 | 129¾ lb. |
| 33 | 132¼ lb. |
| 36 | 133½ lb. |
| 38 | 134¼ lb. |
| 40 | 135 lb. |
| 41 | 135¾ lb. |
| 42 | 136¼ lb. |
| 43 | 136 lb. |

43 weeks. Artificial rupture of membranes. No result.
Medical induction. No result.

Labour 9 days after artificial rupture of membranes - 44th week.

| | | |
|---|---|---|
| 26.9.53. | 8 p.m. | Labour began. |
| 27.9.53. | 4.35 a.m. | Cervix three-quarters dilated.<br>Head occipito anterior.<br>Clear liquor.<br>Foetal heart 136 per minute. |
| | 7 a.m. | Second stage.<br>Foetal heart 120 per minute. |
| | 7.10 a.m. | Foetal heart 120 per minute.<br>Caput advancing. |
| | 7.15 a.m. | Foetal heart 100 per minute. |
| | 7.20 a.m. | Foetal heart not heard. |
| | 7.45 a.m. | Spontaneous delivery after episiotomy of stillborn child weighing 7 lb. 15 oz.<br>Crown-heel length 52 cm.<br>Child covered with meconium and placenta stained with meconium. |

Case No. 1 (continued)

P.M. 387/53.
Histology: A gross bilateral pneumonia of intra uterine origin.

Comment:

Typical postmature syndrome. Death of the foetus without warning in the second stage of a short labour. The histological appearances seen in Fig. 73 are typical of an intra uterine inhalation pneumonia slightly altered by postmortem changes. It is very uncommon to find organisms in the lung in such a case, but the association with 9 days of ruptured membranes might predispose to infection of the amniotic sac. Had severe anoxia not occurred, the foetus would not, of course, have inhaled this material.

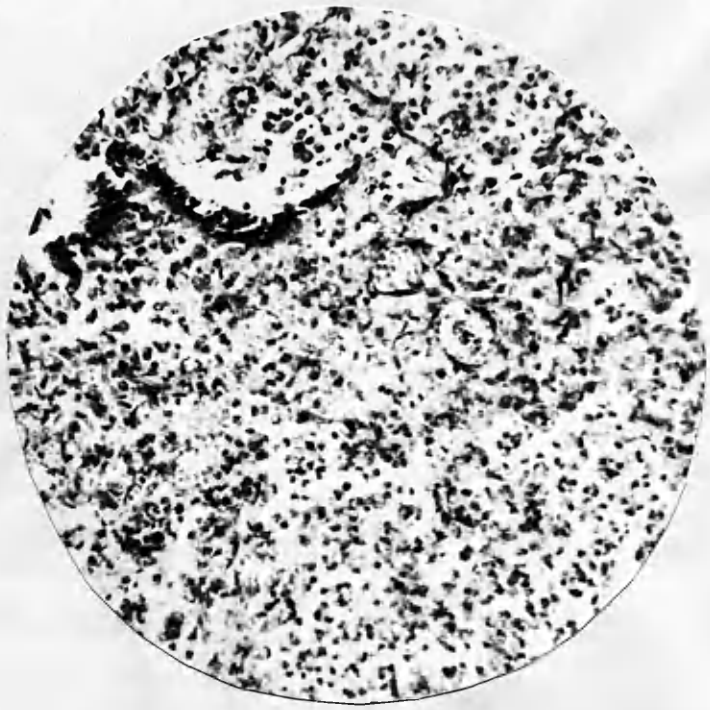


Fig. 73. Foetal lung x 200.
Extensive histological pneumonia.

CASE NO. 2

## POSTMATURE NEONATAL DEATH DESPITE ELECTIVE CAESAREAN SECTION.

No. 2751/48. Primigravida. Aged 35. Height 5'4½".

Attended ante natal clinic from 8th week.

| Weeks. | Maternal Weight. | |
|---|---|---|
| 8 | 101¼ lb. | |
| 12 | 106¼ lb. | |
| 17 | 113¼ lb. | |
| 23 | 122¼ lb. | |
| 26 | 127 lb. | |
| 31 | 132 lb. | |
| 33 | 134½ lb. | |
| 37 | 140¼ lb. | |
| 39 | 141 lb. | |
| 40 | 140 lb. | |
| 41 | 139½ lb. | |
| 42 | 139½ lb. | |
| 43 | 135½ lb. | Ante Natal Admission. |
| Admitted at 43rd week. | | |
| 44 | 134 lb. | |

Examination:

No clinical evidence of liquor amnii.
Uterus wrapped round child.
Cervix thinned out over head.
Cervical os high, posterior, soft and finger easily inserted.
No liquor was obtained when artificial rupture of membranes was attempted.

Elective Lower Segment Caesarean Section.

Spinal Anaesthesia.

Uterus dry.
Child limp and covered with meconium.
Indentation marks on child by compression of uterine wall.
Skin beginning to peel.

Case No. 2 (continued)

Child:

Male. Weighed 6 lb. 12 oz. Crown-heel length 51.5 cm.
Was transferred to Special Nursery for care.
Air entry fair in chest. Moist sounds at bases.
On continuous oxygen and antibiotics.
Remained cyanosed, if out of oxygen, and deteriorated steadily till death occurred at 15 hours.

P.M.

Lungs congested. Meconium in stomach.

Histology:

Lung well aerated.
Evidence of inhaled amniotic sac cells.
Central necrosis of liver.

Comment:

An extreme case of postmaturity, where labour had failed to rescue the foetus before severe anoxia had occurred. The lack of liquor, the desquamation of the skin with indentation marks on the child, and the falling maternal weight over the last four to five weeks are typical, of the syndrome. Caesarean Section was performed too late to save the child.

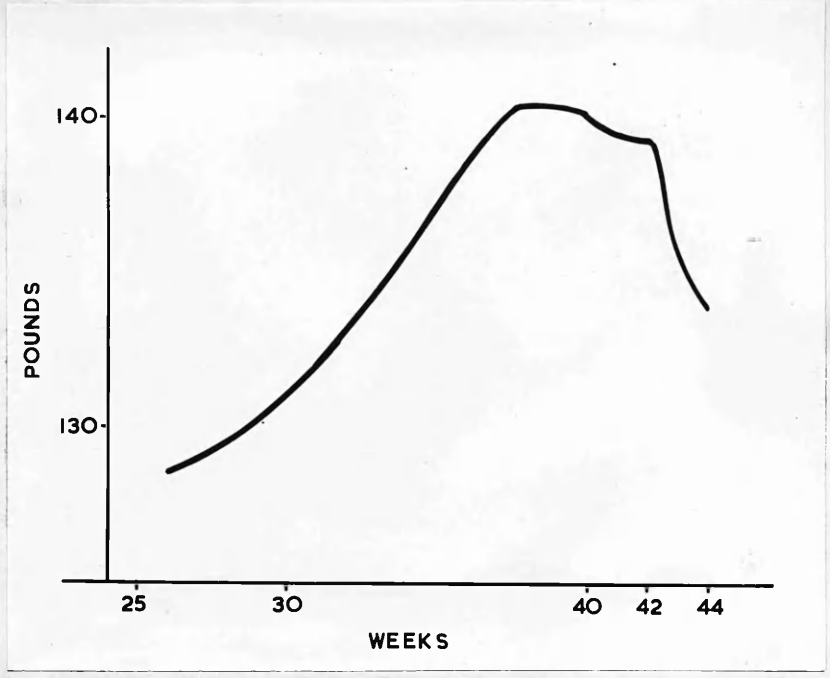



Fig. 74. Maternal Weight Curve. Case No. 2 (2751/48)

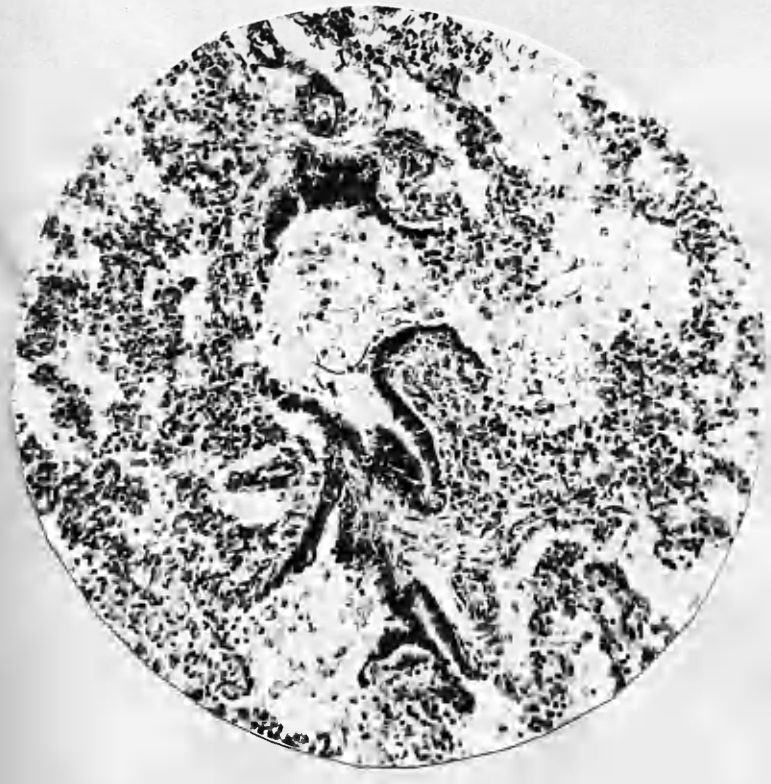


Fig. 75.
Foetal Lung x 200.
Case No. 2 (2715/48)

Inhalation of squames from amniotic sac and primary atelectasis.

## CASE NO. 3.

## TYPICAL POSTMATURE NEONATAL DEATH IN MULTIGRAVIDA

No. 1333/51. Aged 38. 4th Pregnancy.

Obstetric History:

1933. Aged 20. At home. 72 hours labour. Spontaneous Delivery. Child 9 lb. alive.
1940. At home. 12 hours labour. Spontaneous Delivery. Child 9 lb. alive.
1948. 3 months miscarriage.

1951.

Attended ante natal clinic from 14th week.

| Weeks. | Maternal Weight. | |
|---|---|---|
| 14 | 127½ lb. | |
| 19 | 131¼ lb. | |
| 27 | 140¼ lb. | |
| 30 | 143¼ lb. | |
| 33 | 145¾ lb. | |
| 36 | 148¾ lb. | |
| 38 | 149¾ lb. | |
| 40 | 150¾ lb. | |
| 41 | 149¼ lb. | B.P. 130/100 |
| 42 | 152 lb. | B.P. 150/ 98 Oedema ankles. |

Admitted at 42 weeks in labour.

| | |
|---|---|
| 3 p.m. | Labour began. |
| 5.55 p.m. | Admitted to hospital. |
| 6.20 p.m. | Foetal heart strong and regular at 96 per minute. |
| 6.30 p.m. | Membranes intact.<br>Cervix 2 fingers dilated.<br>Artificial rupture of membranes attempted.<br>No liquor was obtained but only thick brown meconium.<br>Oxygen 4 litres per minute to mother by B.L.B. mask. |
| 6.45 p.m. | Foetal heart 136 after 10 minutes - drop to 104 after 10 minutes without oxygen. |

Case No. 3 (continued)

| | |
|---|---|
| 7 p.m. | Foetal Heart 104. |
| 7.15 p.m. | Foetal Heart 118. |
| 7.30 p.m. | Foetal heart strong and regular, 120 per minute. |
| 7.40 p.m. | Spontaneous delivery. |

Child:

Female. Weight 7 lb. 2½ oz.
Trachea full of meconium.
Haemoglobin in cord blood 130 per cent.
Continuous oxygen.
Steady breathing but with subcostal indrawing.
Fine crepitations at lung bases.
Died at 19¼ hours, after a few hours of cyanosis.

Comment:

Typical postmature neonatal death following acute anoxia in labour.

The first labour, although long, ended well, probably because the mother was young, 20 years of age. By the time the third child was born she was 38 years of age and postmaturity at this age is dangerous. The loss of weight after term was masked by mild pre-eclampsia which may have in some measure contributed to the fatal outcome.

CASE NO. 4.

POSTMATURITY PLUS PRE-ECLAMPSIA.

2202/50. Primigravida. Age 30. Height 5'6".
Physical Grade above average.

Attended ante natal clinic from 16th week. E.D.D. 2.9.50.

| Week. | Maternal Weight. | | |
|---|---|---|---|
| 16 | 151½ lb. | | |
| 18 | 155¼ lb. | | |
| 22 | 162½ lb. | | |
| 25 | 168¼ lb. | | |
| 30 | 178½ lb. | | |
| 34 | 184¾ lb. | | |
| 37 | 189¼ lb. | | |
| 39 | 188¾ lb. | | |
| 40 | 193½ lb. | B.P. 145/100. | Oedema. No albumen. |
| 41. Admitted. | 193¾ lb. | B.P. 138/90. | Oedema. Esbach 1 part. |

7.9.50. Medical Induction - failed.

11.9.50. Artificial rupture of membranes.

Labour within 24 hours.

Labour:

| | |
|---|---|
| 9 a.m. | Labour began. |
| 11 a.m. | Foetal heart rate 144 per minute and regular. |
| 1.30 p.m. | Blood pressure 160/100.<br>Cervix 2 fingers dilated.<br>No foetal heart heard. |
| 6.45 p.m. | Spontaneous delivery of stillborn child weighing 6 lb. 14½ oz.<br>3 ounces thick meconium followed the child. There was no liquor amnii. |

Case No. 4 (continued)

P.M. 397/50.

Pia-arachnoid congestion. Tardieu spots heart.
Petechiae in lung.
Meconium stained mucus in trachea and bronchi.

Comment:

Moderate pre-eclampsia (note rapid increase in weight), with superimposed postmaturity. Artificial rupture of the membranes one to two weeks earlier might have saved the child. Either pre-eclampsia or the postmaturity alone not sufficient to cause severe anoxia, but together were lethal.

CASE NO. 5.

## THREATENED ABORTION
## LATE PREGNANCY ANOXIC NEONATAL DEATH

2325/51. Primigravida. Aged 29. Height 5'1½"

Attended ante natal clinic from 21st week.

| Week. | Maternal Weight. |
|---|---|
| 21 | 136¾ lb. |
| 22 | Pain with bleeding. 4 days in bed at home. |
| 24 | 137 lb. |
| 25 | 138¼ lb. |
| 29 | 144 lb. |
| 33 | 146 lb. |
| 35 | 147 lb. |
| 38 | 147¼ lb. |
| 40 | 147½ lb. |

**Labour:**

Spontaneous onset in 41st week.

**27.9.51.**

| | |
|---|---|
| 2 p.m. | Onset of labour. |

**28.9.51.**

| | |
|---|---|
| 5.30 a.m. | Admitted to hospital. |
| 6.5 a.m. | Cervix 2 fingers dilated. |
| 9.15 a.m. | Spontaneous rupture of membranes. Liquor meconium stained. Foetal heart 120 and regular. |
| 9.25 a.m. | Caput showing in distance. Foetal heart 104-112. Oxygen to mother B.L.B. mask (4 litres per minute). |
| 9.35 a.m. | Foetal heart 96 per minute. |
| 9.45 a.m. | Foetal heart 96 per minute. |
| 9.55 a.m. | Episiotomy. Spontaneous Delivery. Male child weighing 7¼ lb. in poor condition. |

Case No. 5. (continued)

Child:

Loose meconium stained mucus was extracted from trachea.

11.20 a.m.

Grunting respiration with marked movement of accessory muscles and poor air entry to lungs. Streptomycin and penicillin were given, and the infant was kept in a 60 per cent. oxygen atmosphere. For 10 minutes in every hour carbon dioxide was allowed to mix with the oxygen as a respiratory stimulant.

Next Day:

There was slight air entry, especially to the left lung, but the child died at 30 hours.

P.M. 414/51.

Crown-Heel Length 50.5 cm.
Culture and smear of lung tissues - no organisms.
Lungs - consolidated with anterior surfaces aerated.
- parenchyma mottled grey-green.
Stomach - multiple small erosions.
Brain - slight subdural bleeding with oedema of extra dural tissues.

Histology Lung:

Inhaled material. Hyaline membrane with plugs in bronchioles. Pneumonia in patches.

Comment:

Threatened abortion early in pregnancy, with acute anoxia manifest in labour at 41st week. No real improvement with oxygen to mother. Typical lung picture at postmortem. Evidence of several types of inhalation picture (see Fig. 76 a - d). Forceps delivery might have saved child but the second stage lasted only 20 minutes. Note the absence of weight gain from the 35th week. Slowing of the foetal heart rate after meconium staining indicates very severe anoxia.

Fig. 76.
Foetal Lung x 200.
Case No. 5 (2325/51)

(a) Hyaline membrane.

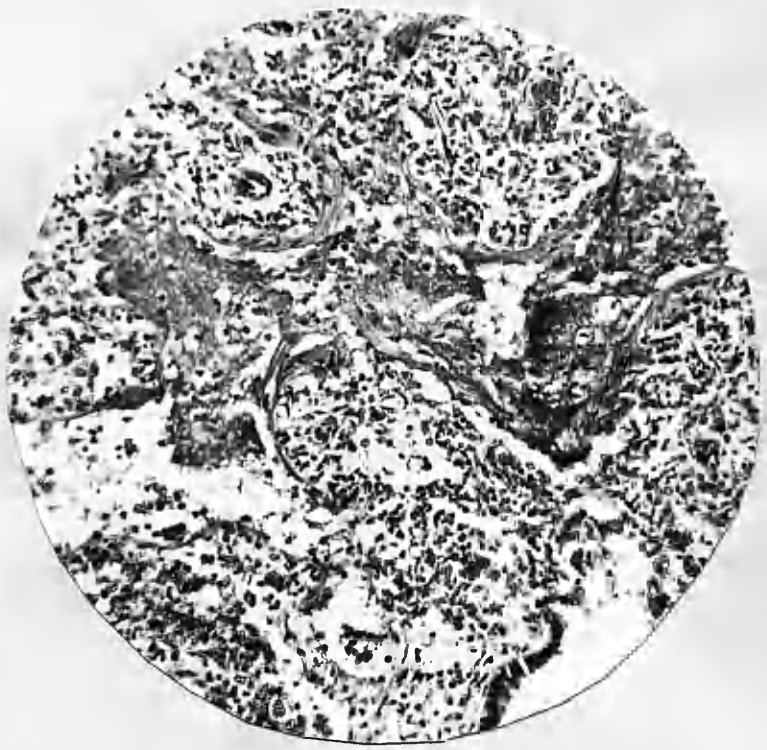


Fig. 76.
(b) Hyaline plugs in air passages.

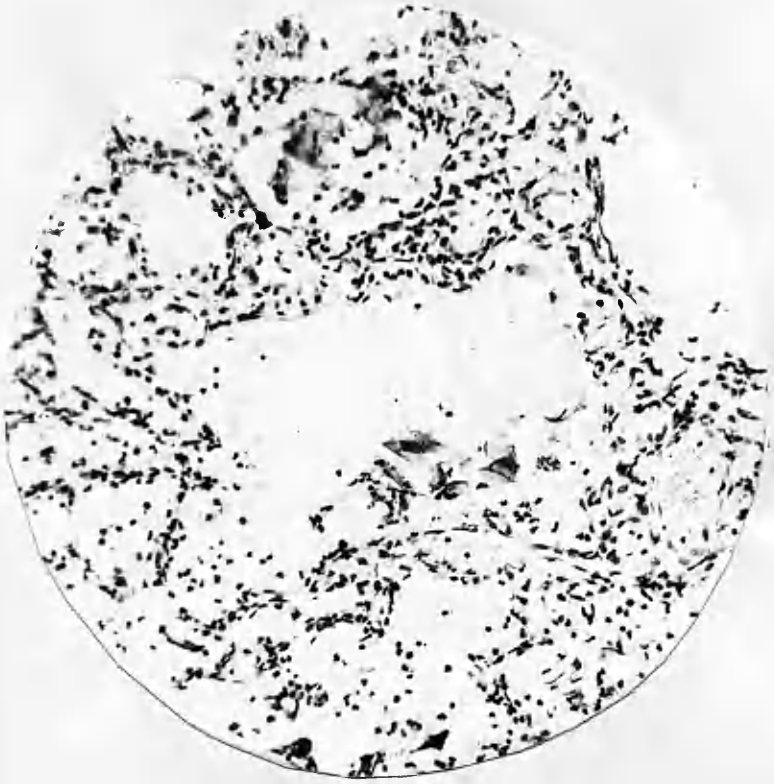


Fig. 76.
(c) Inhaled amniotic squames.

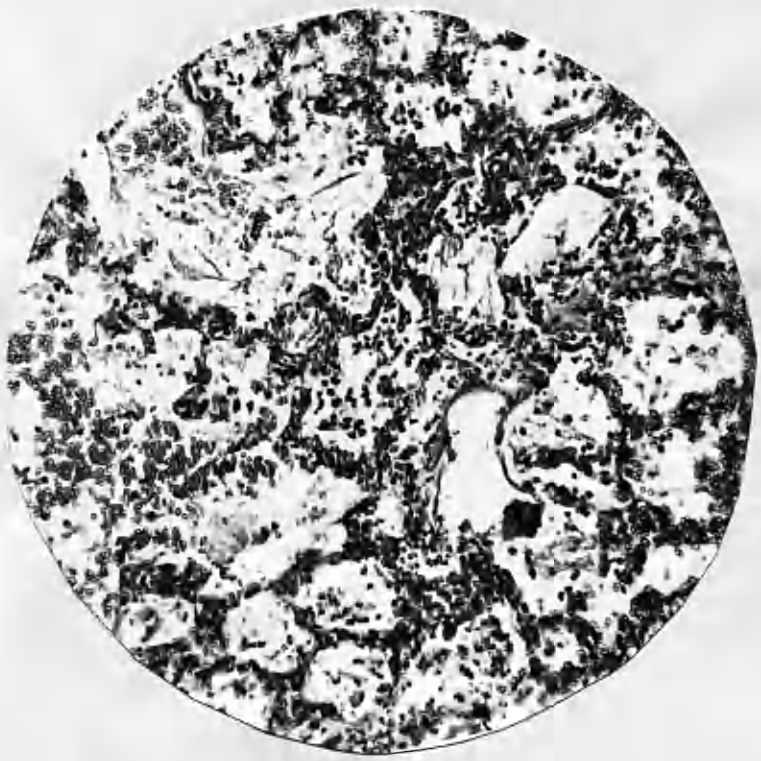


Fig. 76.
(d) Histological pneumonia and haemorr-:hage into air sacs.

Case No. 6 (continued)

P.M. 159/49.

Widespread asphyxial petechial haemorrhages.
Nothing else.

Comment.

Postmature intra uterine death from anoxia in labour. Shows the unreliability of foetal heart rate as a guide to anoxia in such cases. Caesarean Section 24 hours before would have saved the child.

# CASE NO. 7.

## POSTMATURITY
## NEONATAL DEATH DESPITE CAESAREAN SECTION
## (StrA)

13172. Primigravida. Aged 37.

Attended ante natal clinic from 13th week.
Pregnancy normal till 41st week, when she was admitted with slight vaginal bleeding. Examination disclosed no placenta. Over the next three weeks, 3 medical inductions were given without success.

44th week.

| | | |
|---|---|---|
| 4.2.45. | 2 p.m. | Onset of labour. |
| 5.2.45. | 7 a.m. | Pains still first stage.<br>Foetal heart has been normal and regular. |
| | 10.30 a.m. | Spontaneous rupture of membranes with meconium stained liquor.<br>Foetal heart regular at 140 per minute. |
| | 11.25 a.m. | Foetal heart regular at 120 per minute. |
| | 11.30 a.m. | Lower Segment Caesarean Section, under spinal anaesthesia. Head free.<br>No moulding. Child covered with thick meconium. Weight 7 lb. 11¼ oz.<br>In poor condition. |
| | Child: | Resuscitated - aspiration of a lot of meconium from nasopharynx.<br>Breathed only after oxygen and carbon dioxide by intratracheal catheter.<br>Colour never remained good and much meconium was aspirated.<br>Died aged 4¼ hours. |

P.M. 41/45.
Asphyxia with inspiration of liquor amnii and much meconium.

Comment:

Child was adequately dealt with after birth with resuscit-:ation in the head-low position. Extreme inhalation of amniotic sac contents had, however, occurred and adequate pulmonary aeration was not possible. Typical postmature death. Note the complete inadequacy of the foetal heart as a guide to serious anoxia.

## CASE NO. 8.

## CEREBRAL HAEMORRHAGE SUPERIMPOSED ON A SEVERE DEGREE OF LOCAL AND GENERAL ANOXIA.

2517/48. Primigravida. Aged 28. Height 5'4".

Attended ante natal clinic from 15th week.

| Weeks. | Maternal Weight. | |
|---|---|---|
| 15 | 124 lb. | |
| 21 | 129 lb. | |
| 25 | 136 lb. | |
| 29 | 146 lb. | |
| 33 | 150 lb. | |
| 34 | 153 lb. | |
| 36 | 162 lb. | |
| 37 | 163 lb. | |
| 38 | 164 lb. | |
| 39 | 165 lb. | Trace œdema. |
| 40 | 158 lb. | (In hospital). |
| 41 | 158 lb. | |
| 42 | 156½ lb. | B.P. 140/90. |

Admitted on dates because of oedema.

| | |
|---|---|
| 20-21.10.48. | Medical Induction. |
| 24-25.10.48. | Medical Induction. |
| 27.10.48. | Artificial rupture of membranes. |
| 29.10.48. | Medical Induction. |
| 29.10.48. | |
| 2 p.m. | Labour began. |
| 7.35 p.m. | Cervix thin, stretched over head. Pinhole os. Head deep in pelvis in occipito-lateral position. No disproportion. |
| 30.10.48. | |
| 6.45 p.m. | Thick meconium. Foetal heart 160 per minute and regular. Cervix unchanged. |
| 31.10.48. | |
| 7.15 a.m. | Meconium staining still present. Foetal heart 150 and regular. |

Case No. 8 (continued)

31.10.48.
1 p.m.

Cervix 2 fingers dilated and thin.
Marked moulding of foetal head.
Head in the right occipito-lateral position, deep in pelvis.
Forceps delivery moderately easy after dilatation and incision of cervix.
Child stillborn, weighing 7 lb. 1½ oz. and of 50 cm. crown-heel length.
Thick light-green meconium followed the child.

P.M. 392/48.

Brain substance extremely congested with rupture of great vein of Galen at junction of straight sinus.

Lungs full of green mucus. Typical petechiae asphyxial haemorrhages.

Comment:

Anoxia in labour from defective placental transfer manifest by meconium. No evidence of foetal heart slowing. Moderately difficult delivery superimposed on anoxia sufficient to kill foetus. Death probably mainly anoxic but added cerebral haemorrhage from minimal trauma. Caesarean Section should have been performed 24 hours earlier in the labour.

## CASE NO. 9.

## BREECH - CORD ENTANGLEMENT TR. (CORD).

10709. Primigravida. Aged 23 years.

Attended ante natal clinic from 10th week.

Spontaneous onset of labour, with the child presenting as a breech, in the 41st week.

First stage of labour lasted 6½ hours.

| | |
|---|---|
| 2.15 p.m. | At onset of 2nd stage.<br>Foetal heart 134 per minute, regular. |
| 2.30 p.m. | Foetal heart 120 per minute, regular. |
| 3.15 p.m. | Foetal heart only 110 per minute.<br>Breech with extended legs in mid pelvis. |
| 3.20 p.m. | Foetal heart 70 per minute. |
| 3.25 p.m. | Foetal heart 60 per minute. |
| 3.30 p.m. | Breech extraction, easy.<br>Cord was coiled round leg, neck and shoulders tightly, but was not pulsating.<br>Forceps to aftercoming head.<br>Child weighed 7 lb. 2 oz. and was stillborn. |

P.M. 330/43.
Bilateral tentorial tear with extensive haemorrhage.

Comment:

Child was dead before it had reached brim of pelvis and certainly before forceps applied. Probably haemorrhage and tear secondary to minimal trauma on a dead foetus with cerebral congestion following acute cord occlusion. The foetal heart picture is fairly typical of acute cord occlusion.

## CASE NO. 10.

## MULTIGRAVIDA - HISTORY OF STILLBIRTHS.

813/50. Primigravida. Aged 31. Height 5'3".

Slight pre-eclampsia at 37th week, settled in hospital. Blood pressure had been normal for 7 days. Spontaneous onset of labour 41 weeks. Intra uterine death after 50 hours in first stage. Child - male, 7 lb. 6¼ oz., covered with meconium at delivery.

P.M. Acute asphyxial death. Inhaled debris. Histological pneumonia.

2334/51. 2nd Pregnancy. Aged 32.

Attended ante natal clinic. Blood pressure normal. Admitted on the estimated date of delivery. Medical induction failed. Artificial rupture of membranes at 42 weeks. A few drops of brownish liquor obtained. Labour within 12 hours.

| | |
|---|---|
| 8.45 a.m. | Labour began. |
| 10.45 a.m. | Meconium staining.<br>Foetal heart 144 per minute.<br>Oxygen to mother at the rate of 4 litres per minute by B.L.B. mask. |
| 11.25 a.m. | Meconium staining.<br>Foetal heart 150 per minute.<br><br>Foetal heart, at ½-hourly intervals, 140-150, regular. |
| 1.40 p.m. | Foetal heart 120 per minute, regular. |
| 2.15 p.m. | Foetal heart 116 per minute, regular. |
| 2.35 p.m. | No foetal heart heard - onset of second stage. |
| 3.5 a.m. | Spontaneous delivery of stillborn child weighing 7 lb. 10 oz. and of 53 cm. crown-heel length. |

P.M. 429/51.

Trachea and bronchi plugged with meconium and mucus. Large bowel empty of meconium.

Comment:

Previous history of stillbirth - more likely to have anoxia in second pregnancy. Postmaturity with lethal anoxia. No guidance from foetal heart.

Case No. 10 (continued).

2454/52. 3rd Pregnancy. Aged 33 years.

Dates very doubtful; only two visits to ante natal clinic. Admitted in second stage - Assisted Breech Delivery of a live child weighing 7 lb. 10 oz.

2678/53. 4th Pregnancy. Aged 34 years.

No clinic visits. No ante natal care.

Admitted at 40th week in late first stage of labour. Foetus lying transversely with an arm and the umbilical cord prolapsed in the vagina. The foetal heart was regular at 112 per minute, but there was meconium staining. Internal version and breech extraction of stillborn child weighing 7 lb. 13¼ oz. and 52 cm. crown-heel length.

P.M. 411/53.
Death due to tentorial tearing with subdural haemorrhage, but with associated signs of anoxia.

Comment:

An interesting history showing the constitutional risk of stillbirth in a given patient. All three deaths associated with anoxia. The first associated with mild pre-eclampsia, the second with postmaturity and the third with superimposed trauma.

## CASE NO. 11.

## TYPICAL "UNEXPLAINED" MECONIUM STAINING.

No. 1596/53. Primigravida. Aged 37 years.
Height 5 feet 2¼ inches.
Married 12 years.

Attended ante natal clinic from early pregnancy.
Pregnancy normal.
Maternal weight (see Fig. 77).

Artificial rupture of membranes at beginning of 42nd week in view of duration of pregnancy only. Liquor thick with meconium, 15 ounces at least present. Cervix soft and taken up, and one finger easily inserted.

Elective Lower Segment Caesarean Section under spinal anaesthesia - 42nd week.

Child weighed 8 lb. 2 oz. and did well.

Oxygen in Umbilical Vessels.

Capacity 24.6 vols. per cent.

Content -
Vein 7.7 vols. per cent. Artery 1.5 vols. per cent.

Saturation -
Vein 31.4 per cent. Artery 6.0 per cent.

## CASE NO. 11 (contd)

Comment:

Meconium staining of "unexplained" type due to foetal anoxia. Foetal anoxia due to duration of pregnancy and made more severe and occurring earlier because of advancing maternal age. Had this infant been required to undergo the stress of labour, especially a prolonged dysfunction labour, severe anoxia with inhalation of meconium stained liquor would have occurred. (See Case No. 7). The child might have died during labour or neonatally from the effects of this inhalation.

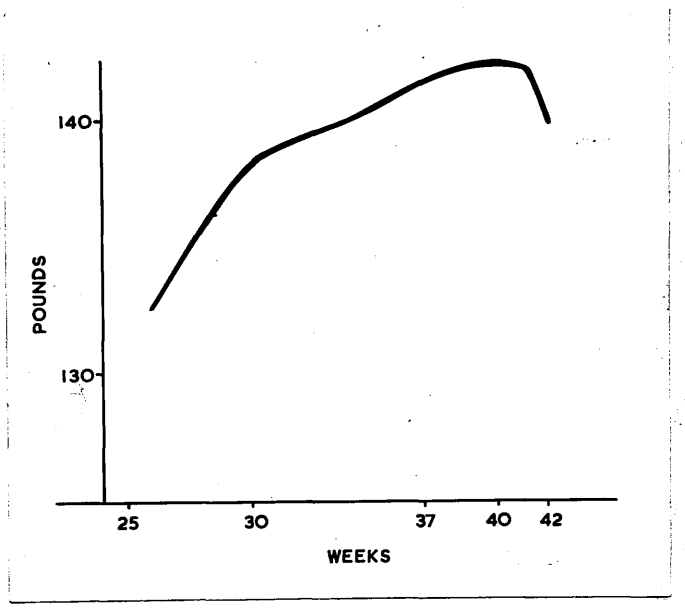



Fig. 77. Maternal Weight Curve.

## CASE NO. 12.

## FOETAL DISTRESS - PRESSURE ON FOETAL HEAD.

3004/50. Primigravida. Aged 21. Height 5'1½"

Ante natal care from 10th week. Pregnancy uneventful.

Spontaneous onset of labour in 42nd week.

**9.12.50.**

| | |
|---|---|
| 4 a.m. | Labour began. |
| 11.20 a.m. | Admitted to hospital. Foetal heart 156 per minute and regular. |
| 3.10 p.m. | Foetal heart 100 per minute with pains, picking up slowly to 120 per minute. |
| 3.30 p.m. | On pelvic examination the head was in the upper pelvis. There was marked moulding. The cervix was only 3 fingers dilated. Uterine pains good with moderately high tone between contractions. |
| 8.20 p.m. | Foetal heart rate continued at 80-96 per minute with pains, rising to 116 between them, but at 8.20 p.m., when the cervix was fully dilated, the rate was 110 per minute between and during pains. |
| 8.52 p.m. | Forceps Delivery. Head in left occipito lateral position in low pelvis. Pelvis in lower diameters roomy, and rotation and forceps delivery fairly easy. |
| Infant: | The infant weighed 7 lb. 10 oz. Moulding excessive - "long head." Crown-heel length was 50 cm. |

Comment:

Irregularity with slowing of foetal heart without meconium staining, probably due to constant squeeze of head with much moulding in brim and upper pelvis.

Improvement in foetal heart in second stage frequently seen as low pelvis often roomy and pressure on head eases off.

CASE NO. 15.

SLOWING FOETAL HEART IN SECOND STAGE.

2467/53. Primigravida. Aged 26 years. Height 5'5". Physical Grade Excellent.

Ante natal care from 16th week.

| Weeks. | Maternal Weight. | | |
|---|---|---|---|
| 17 | 134 lb. | | |
| 21 | 138 lb. | | |
| 25 | 144 lb. | | |
| 28 | 145¼ lb. | | |
| 32 | 148½ lb. | | |
| 34 | 148 lb. | | |
| 36 | 151¼ lb. | | |
| 37 | 151¾ lb. | | |
| 38 | 150 lb. | | |
| 39 | 150¾ lb. | B.P. 136/92. Trace albumen. | In hospital. |
| 40 | 150¾ lb. | B.P. 136/94. No albumen. | |

Spontaneous onset of labour at 40th week.

29.9.53.

10.30 p.m. Pains began.

30.9.53.

12.40 a.m. Foetal heart 136 per minute, regular. Blood pressure 158/100.

1 a.m. Spontaneous rupture of membranes. Foetal heart 130 per minute.

1.20 a.m. Caput showing. Foetal heart 120 per minute, but slightly irregular.

1.30 a.m. Foetal heart 80 per minute with pains. Pains not strong.

1.35 a.m. Foetal heart 46 to 60 per minute with pains. Pains strong.

1.40 a.m. Forceps Delivery. Female child weighing 7 lb. 4½ oz. Excellent response to minimal resuscitation.

Under the influence of the anaesthetic, the foetal head

Case No. 13 (continued)

was in the right occipito lateral position in mid pelvis, but rotated easily down into the occipito anterior position in low pelvis with pressure on the fundus, and forceps were easily applied.

Comment:

Very mild pre-eclampsia in a very fit primigravida. Sudden foetal heart slowing for no apparent clinical reason. There was no mechanical obstruction. Pains were not excessive. Forceps delivery of normal child.

## CASE NO. 14.

## HYPERTENSION - MIXED ACCIDENTAL HAEMORRHAGE - FOETAL DISTRESS

205/50. Primigravida. Aged 36. Height 5'1".
Married 1 year.

Ante natal care - attending general practitioner.

Admitted to Aberdeen Maternity Hospital at 30th week of pregnancy with essential hypertension. Blood pressure 176/126.

| Weeks. | Maternal Weight. | | | |
|---|---|---|---|---|
| 30 | 138½ lb. | B.P. 176/126. | No oedema. | No albumen. |
| 31 | 140 lb. | B.P. 150/ 98. | No oedema. | No albumen. |
| 32 | 140 lb. | B.P. 140/100. | No oedema. | No albumen. |
| 33 | 142 lb. | B.P. 140/ 90. | No oedema. | No albumen. |
| 34 | 144 lb. | B.P. 150/110. | No oedema. | No albumen. |
| 35 | 145 lb. | B.P. 158/120. | No oedema. | No albumen. |
| 36 | 142½ lb. | B.P. 180/130. | No oedema. | Trace albumen. |
| 37 | | B.P. 150/130. | No oedema. | Albumen 1 part Esbach. |

In her 37th week, at 10 p.m. on 21.3.50, she had slight vaginal bleeding followed by generalised abdominal ache. Blood pressure 220/150. Intermittent brisk vaginal bleeding followed. Total loss about 10 ounces. Very little abdominal discomfort. (Mixed accidental haemorrhage).

Foetal heart 110 per minute at first bleeding, but continued good and was 120 per minute and regular just before abdomen incised.

At 11 p.m. 21.3.50, Classical Caesarean Section under general anaesthesia, in an attempt to save the child.

At Operation: Typical accidental haemorrhage with haemorrhage into the uterine muscle and broad ligaments. A "classical" incision was performed and a small child, weighing 3 lb. 7 oz. was extracted as a breech.

The amniotic sac was full of fresh green meconium. The placenta was three-quarters separated by fresh blood clot.

The child was resuscitated with difficulty but ultimately did well. The mother did extremely well, but marked hypertension persisted.

Case No. 14 (continued)

Comment:

From the obstetrical point of view, interference was indicated about 4 or 5 days before haemorrhage occurred, but labour had not been induced since the child was still very small. The main interest in the case is the extensive placental separation with heavy meconium staining but without evidence of foetal heart slowing or irregularity. In other words, severe anoxia is manifest by meconium staining rather than by foetal heart slowing.

CASE NO. 15

INTRA UTERINE ANOXIA

SUBSEQUENT SPASTIC PARALYSIS

1543/46. Second pregnancy. Aged 37 years. Height 5'4".

Obstetric History:

1945. Stillbirth due to eclampsia at the 43rd week of gestation.

27.8.46. Admitted as an emergency in the 42nd week of gestation, in view of history and current postmaturity.

28.8.46. Medical induction, and repeated on 30.8.46.
29.8.46. Artificial rupture of the hindwaters.
10 ounces liquor withdrawn.

31.8.46.

| | |
|---|---|
| 11 a.m. | Onset of labour. |
| | The foetal heart remained strong and regular at 138 to 142 per minute. |
| 6.30 p.m. | Onset of second stage of labour. |
| 7.25 p.m. | Caput just visible. Foetal heart rate suddenly dropped, to 100 per minute. |
| 7.40 p.m. | Delivery by forceps under general anaesthesia. The foetal head was lying with the occiput anterior and delivery was easily effected. A large amount of meconium followed the child, and the umbilical cord was noted to be tightly round the child's neck. |
| The Child: | Weighed 8 lb. 10¼ oz. and was severely asphyxiated at birth. Thick meconium stained mucus was aspirated from the trachea. Grunting respiration established with difficulty. Oxygen given by mask. |
| | Obvious "cerebral" signs for first few days (twitching, alert, etc.) but settled by the 5th day and was discharged apparently well. |

Case No. 15 (continued)

At the age of 5 years was examined by Mr. G.A. Pollock at Westerlea School to assess his fitness to be admitted for special care as a case of spastic paralysis. There was a slight speech and visual defect in addition to generalised spasticity of all four limbs. The lowest limbs were most affected and the left arm least of all. The child was considered to be below the intellectual level which would allow him to be treated at Westerlea.

March, 1952.

Elective Caesarean Section under general anaesthesia at the 39th week of pregnancy. The child was a male, weighing 8 lb., in good condition and did well.

Comment:

The risk of serious anoxia in utero could have been foreseen because of postmaturity, history of postmature stillbirth, and the age of the mother.

Severe anoxia developed during a short and easy labour, possibly accentuated by the previous medical induction. Meconium was not passed externally till the foetus was born and there was therefore no clinical evidence of distress until the late second stage. It is difficult to assess the importance of the cord (round the neck) but it probably was only responsible for trouble late in labour. If an element of ischaemic anoxia was present due to interference with the foetal circulation, this would, of course, have a more severe effect on the brain and may have contributed to the serious outcome.

Obstetrically, induction of labour at term or elective CaesareanSection when first admitted should have been advised.

## (4) PUBLICATIONS.

## PUBLICATIONS.

Certain of the material of this thesis has been published. Much of the rest of the material is in the course of publication, or is being prepared for publication.

(1) Haemoglobin and Red Cells in the Human Foetus and their relation to the oxygen content of the blood in the vessels of the umbilical cord.

Walker, J. and Turnbull, E.P.N. (1953)
Lancet, ii, p. 312. (Copy appended).

(2) "Causes and Prevention of Stillbirth."

Baird, D. and Walker, J. (1954)
Chapter in British Obstetric Practice,
Heinemann, London. (In the press)

(3) Foetal Anoxia. (The Blair-Bell Memorial Lecture, September, 1953).

Walker, J. (1954)
Journ. Obstet. Gynaec. Brit. Emp. (In the press)

(4) "Oxygen Levels in Human Umbilical Cord Blood."
(A Preliminary Communication)

Walker, J. (1953)

Chapter in "Anoxia of the Newborn Infant,"
Blackwell, Oxford.

Paper read at Symposium organised by the Council for International Organisations of Medical Sciences in London, October, 1951.